



FIG. 1

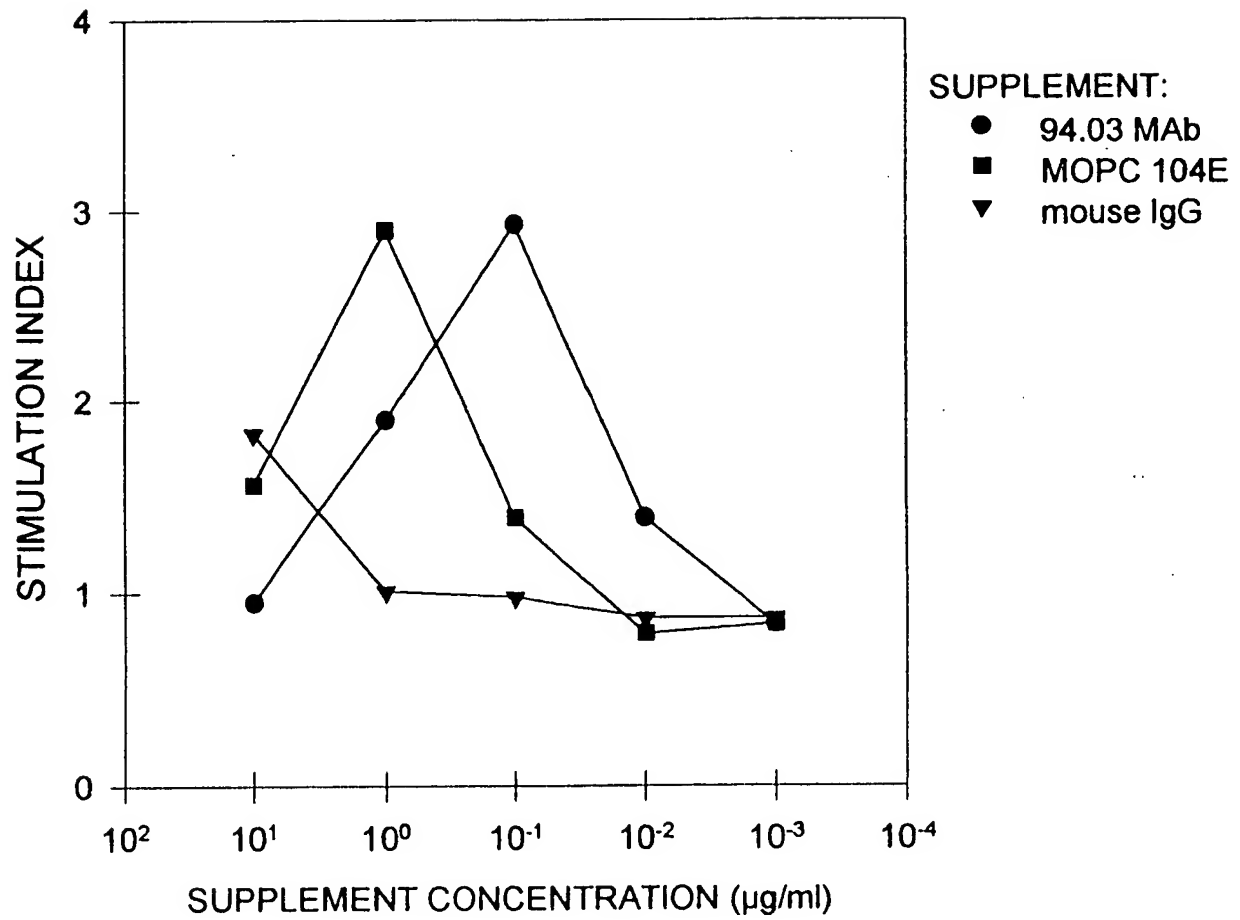
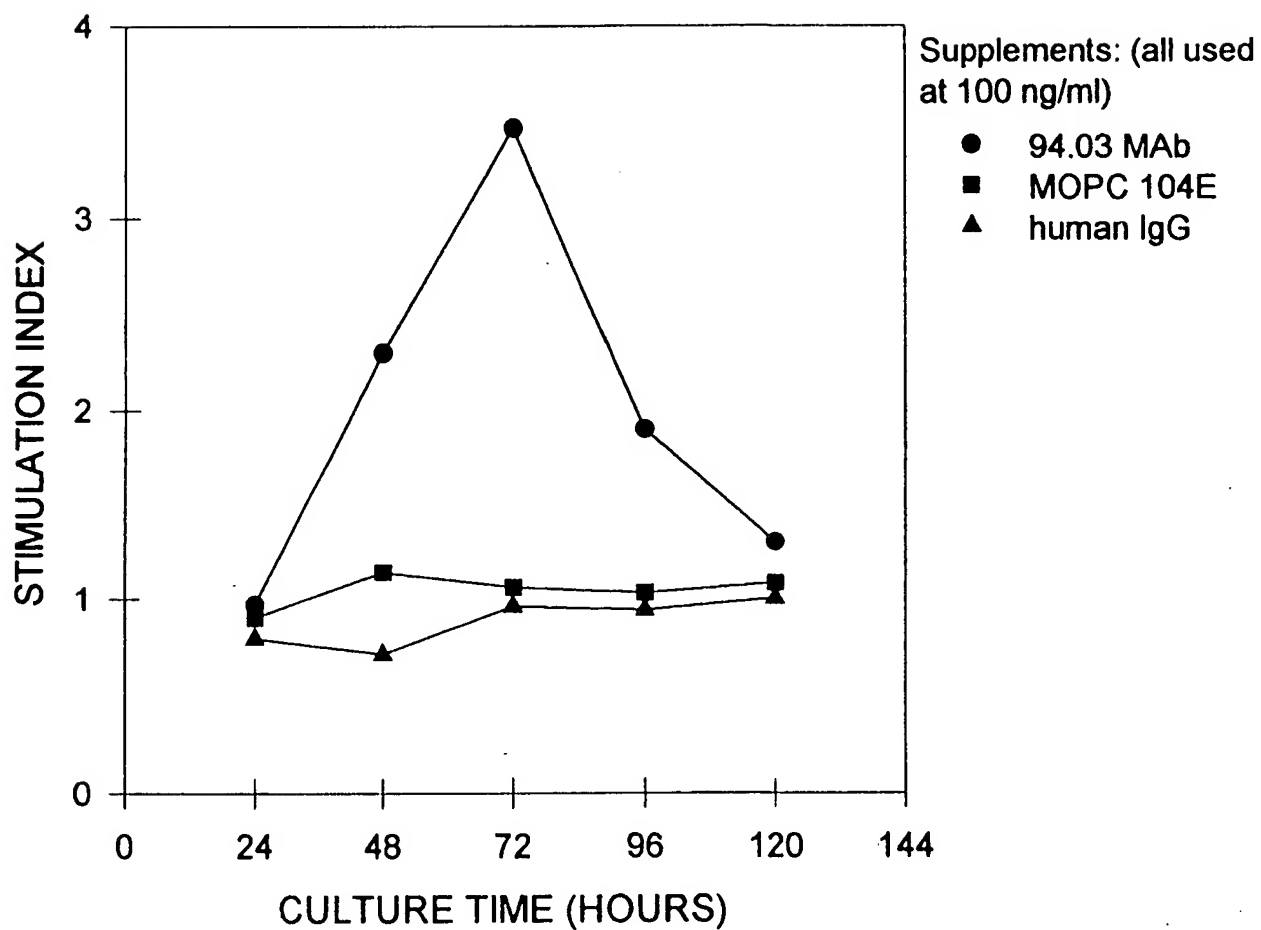
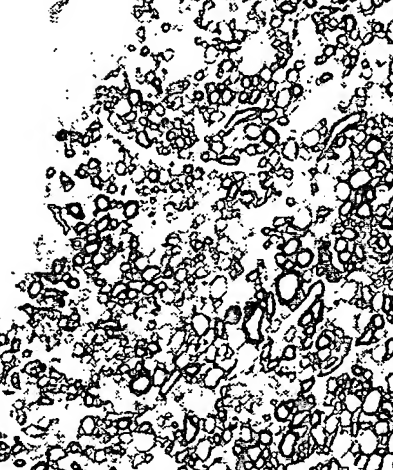




FIG. 2





B

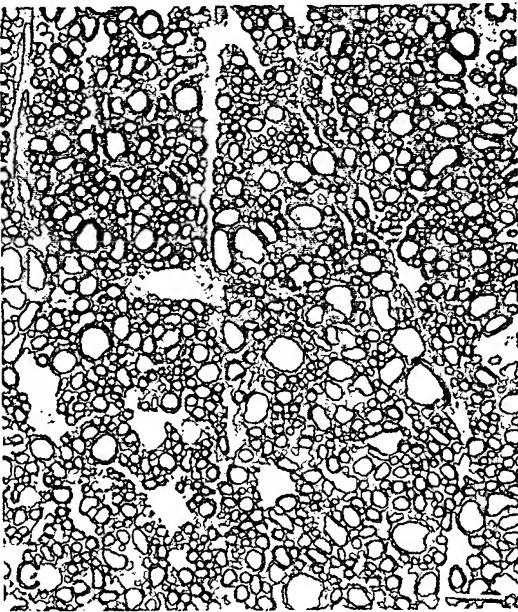


FIG. 3D



FIG. 5

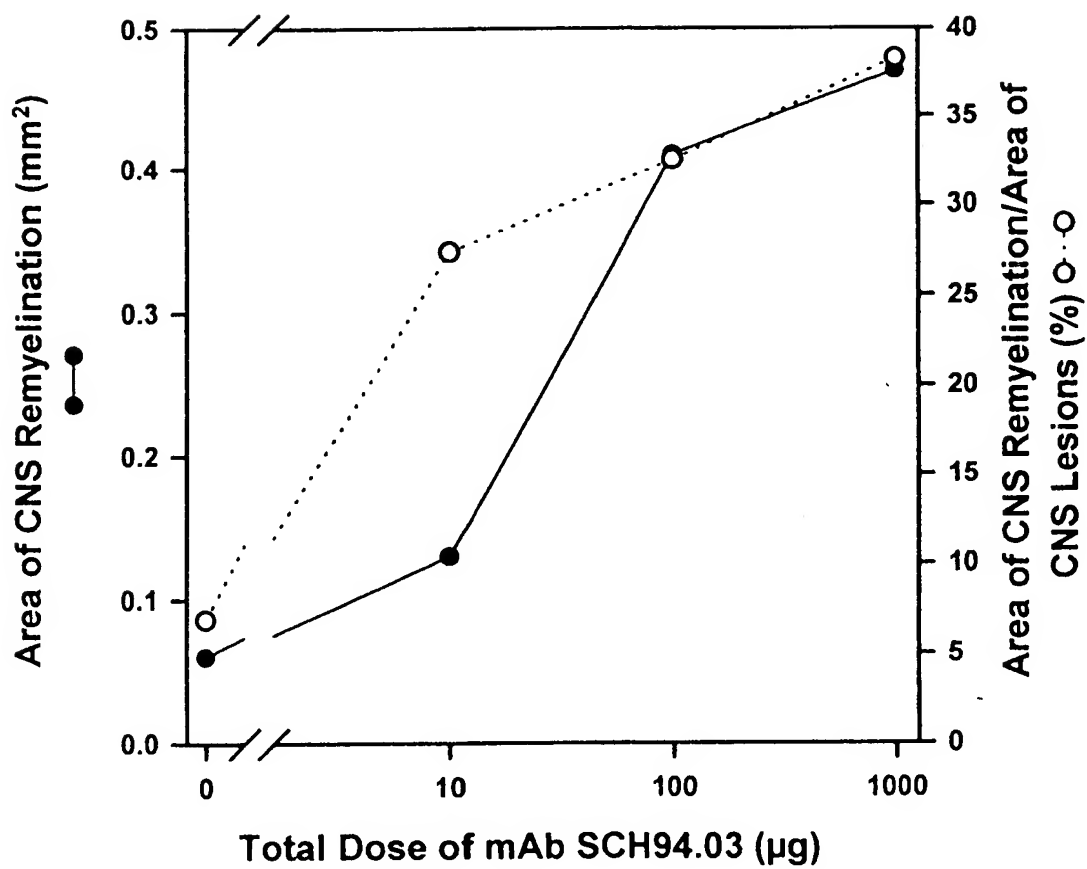
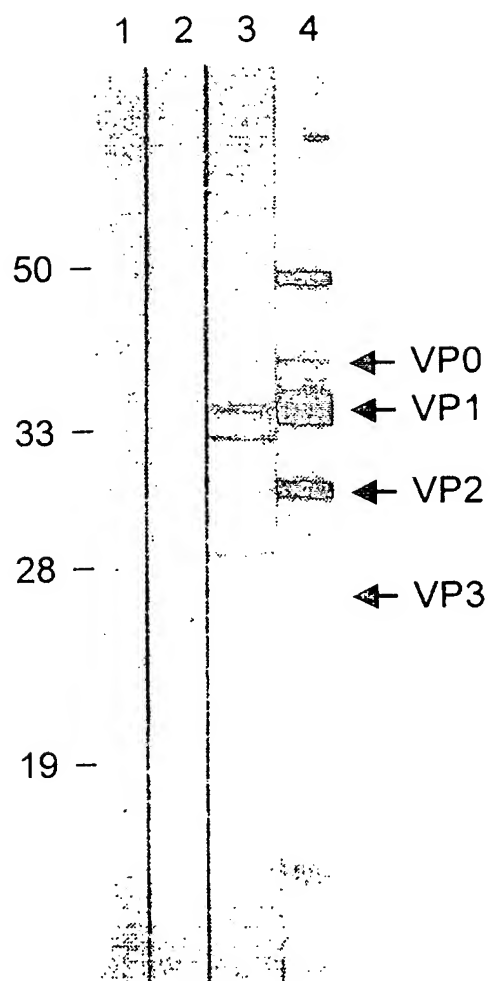


FIG. 6



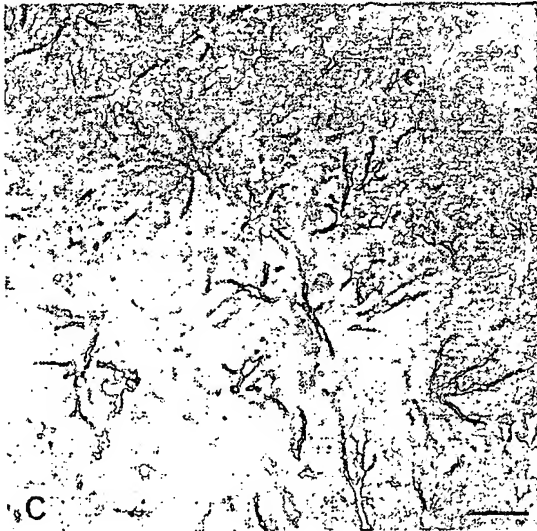


FIG. 7D

Protein antigen ELISA with SCH94.03

FIG. 8A

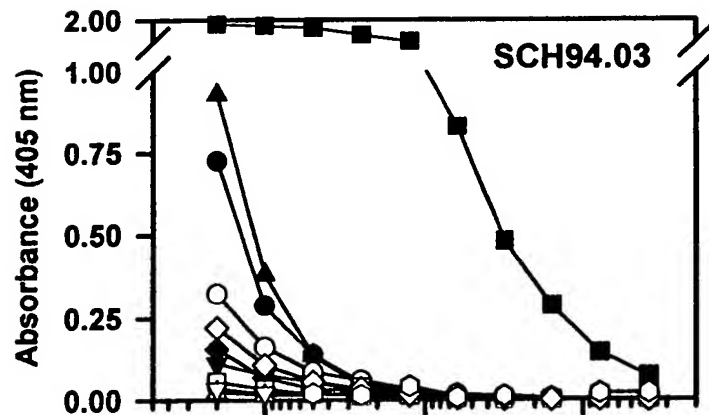


FIG. 8B

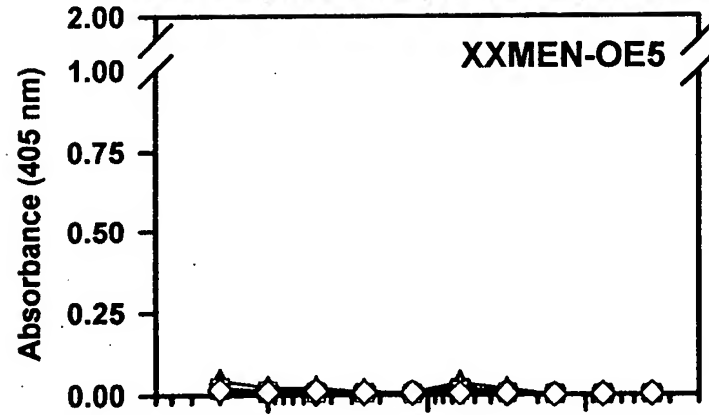
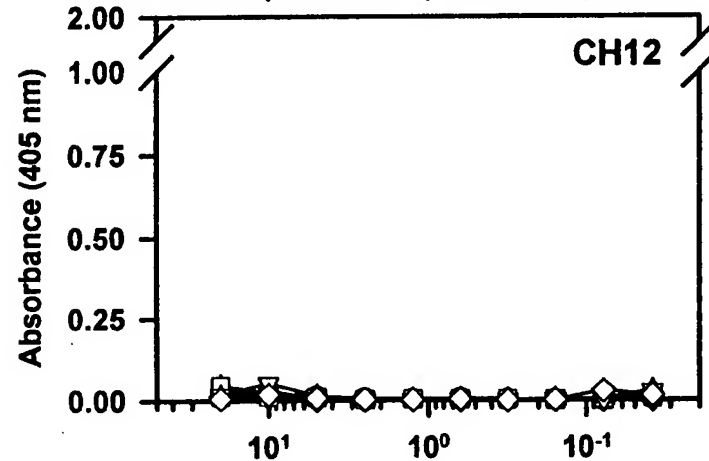


FIG. 8C



Antibody concentration (µg/ml)

Antigen:

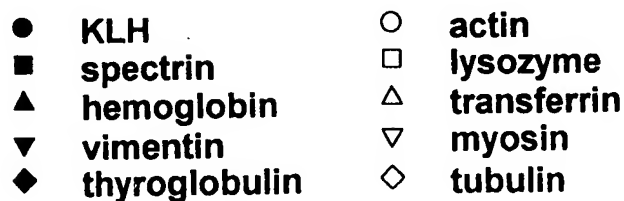




FIG. 9

ELISA with SCH94.03 F(ab₂)' fragments

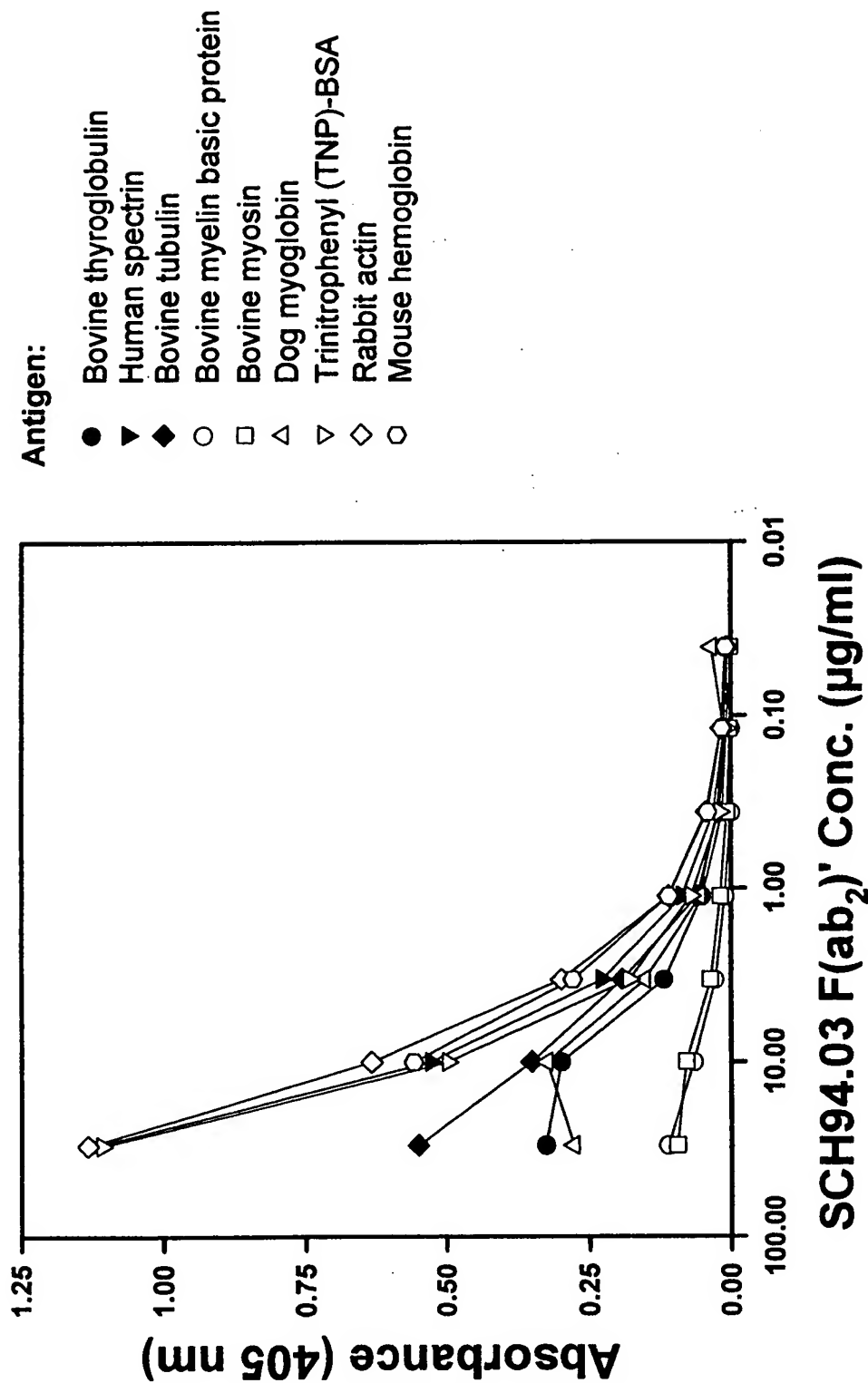


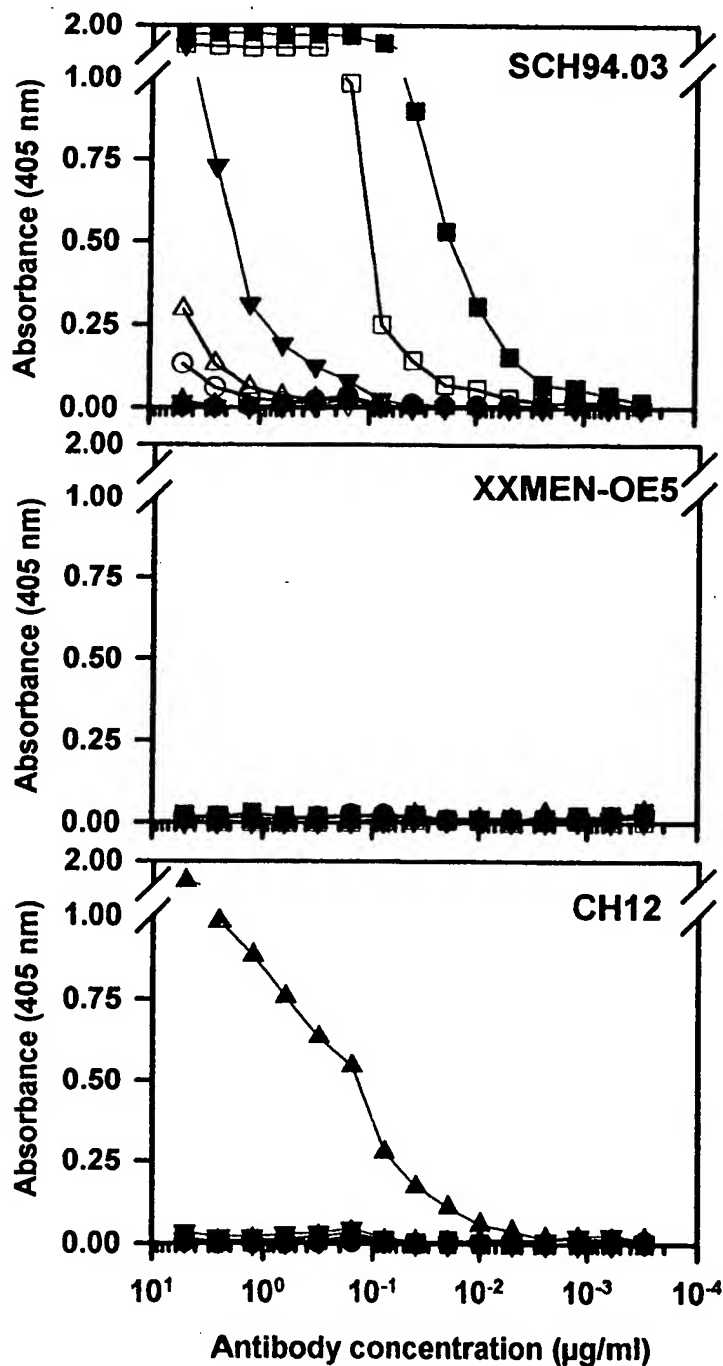


FIG. 10A

FIG. 10B

FIG. 10C

Chemical hapten ELISA with SCH94.03



Hapten:

- | | | | |
|---|------|---|-----|
| ● | none | ○ | Ars |
| ■ | FL | □ | NP |
| ▲ | TMA | △ | TNP |
| ▼ | PhOx | ▽ | PC |

Immunoglobulin Light Chain Variable Region Sequence of SCH94.03

[illegible][illegible][illegible][illegible]

E-1

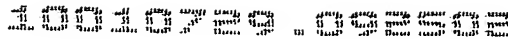


FIG. 11B

	-19	-9	1	
SGH94.03	ATG GGA TGG AGC TGT ATC ATC CTC TTT TTG GTA GCA GCA GCT ACA GGT GTC CAC TCC TCC GTC CAA CTG CAG CAG CCT GGG			
CH12	---	---	---	---
germline V73	---	---	---	---

SCH94.03
CH12
germline

germline v23

CDR1

[illegible]

SCH94.03
CH12
reemline

remlin v23

CDR2

[illegible]

SCH94.03
CH12
germline

germLine v23

CDR2

[illegible]

SCH94.03
CH12
germline

germline v23

CDR3

[illegible]

SCH94.03
CH12
germline

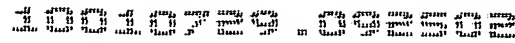
JH2

८

[illegible]

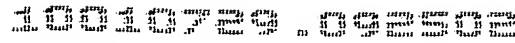
SCH94.03
CH12
germline

gemLine Jy2



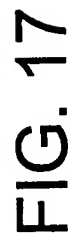
Leader Peptide

[illegible]



Leader Peptide

[illegible]



												-4		+1													
M	E	S	Q	I	Q	V	F	V	F	V	F	L	W	L	S	G	V	D	G	D	I	V	M	T	Q	S	H
ATG	GAG	TCA	CAG	ATT	CAG	GTC	TTT	GTA	TTC	GTG	TTT	CTC	TGG	TTG	TCT	GGT	GTT	GAC	GGA	GAC	ATT	GTG	ATG	ACC	CAG	TCT	CAC

K F M S T S V G D R V S I T C K A S Q D V S T A V A W Y
 AAA TTG ATG TCC ACT TCA GTA GGA GAC AGG GTC AGC ATC ACC TGC AAG GCC ACT CAG GAT GAT GTG AGT ACT GCT GTA GCC TGG TAT

Q Q K P G Q S P K L L I Y S A S Y R Y T G V P D R F T G
 CAA CAG AAA CCT CCT AAA CTA CTG ATT TAC TCG GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT GGC TTC ACT GGC

70										80										90									
S	G	S	G	T	D	T	F	T	F	T	I	S	S	V	Q	A	E	D	L	A	V	Y	Y	C	Q	Q	H	Y	
AGT	GGA	TCT	GGG	ACG	GAT	TTC	ACT	ACT	TTC	ACC	ATC	AGC	AGT	GTG	CAG	GCT	GAA	GAC	CTG	GCA	GTT	TAT	TAC	TGT	CAG	CAA	CAT	TAT	

C region

J region

										100			106			106A		
T	T	P	L	T	F	G	A	G	T	K	L	E	L	K	R			
CTC ACG TTC GGT GCT GGG ACC AAG CTG GAG CTG AAA CGG GCT GAT GCT TCA																		
ACT	ACT	CCG	---	---	---	---	---	---	---	-G-	---	---	---	---	---			

online JxS
BS



FIG. 18

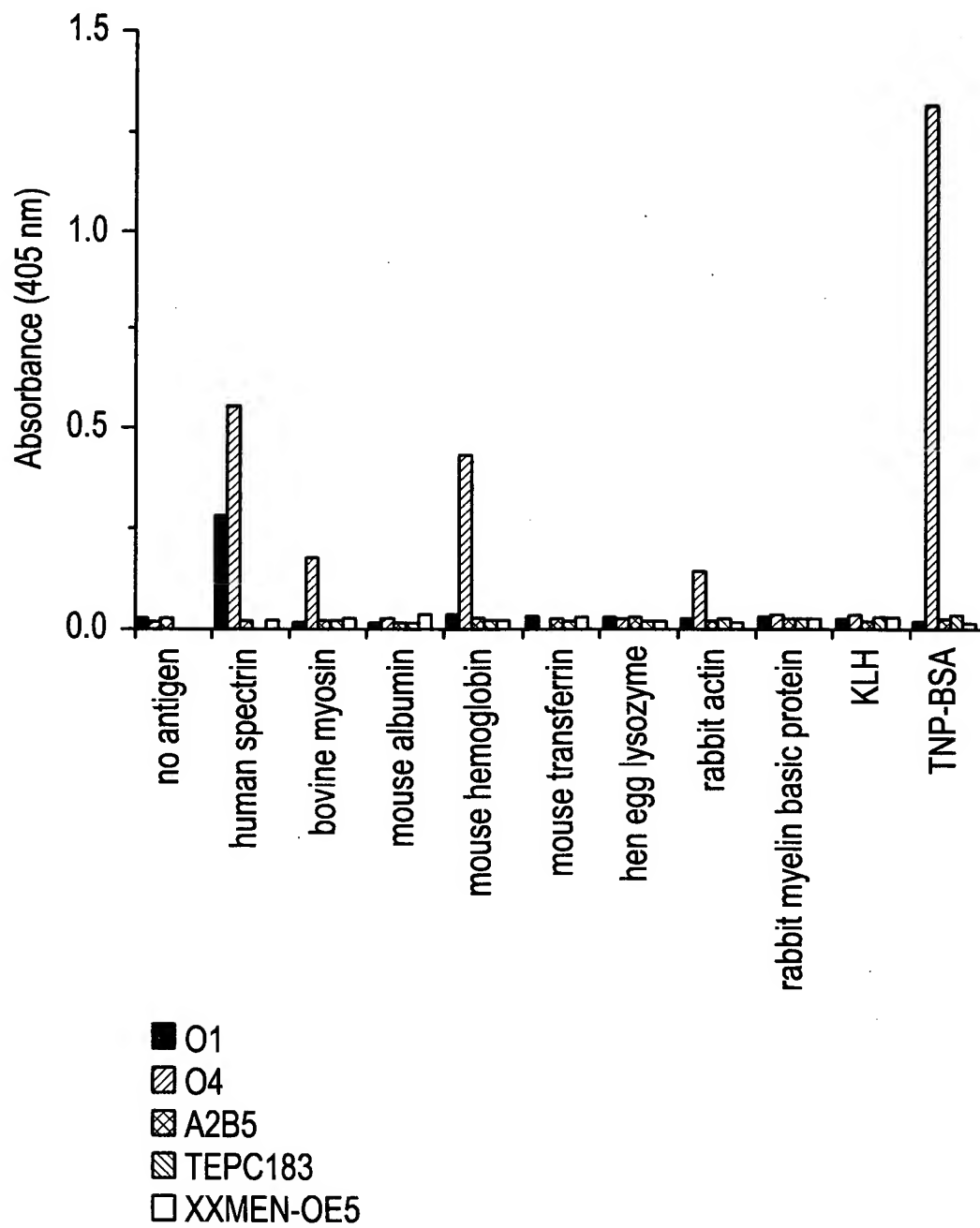


FIG. 19A

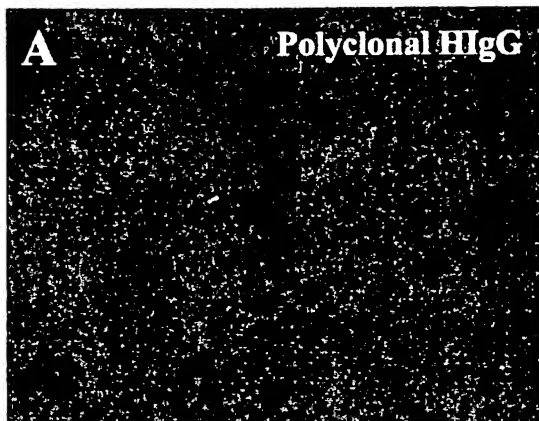


FIG. 19B

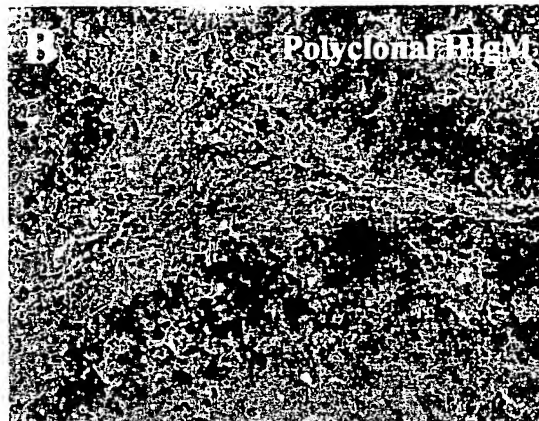


FIG. 19C

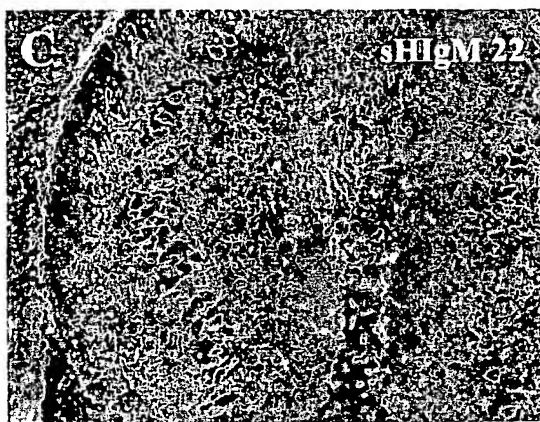


FIG. 19D

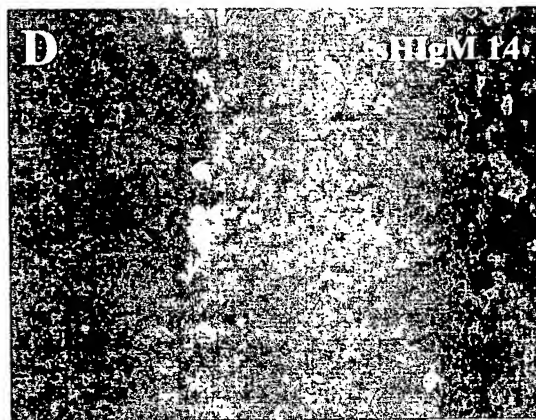


FIG. 19E

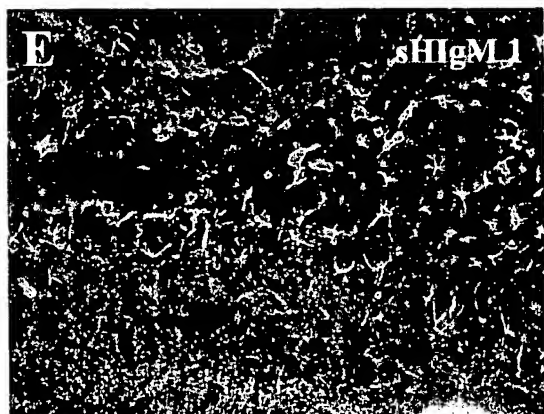


FIG. 19F



FIG. 20A

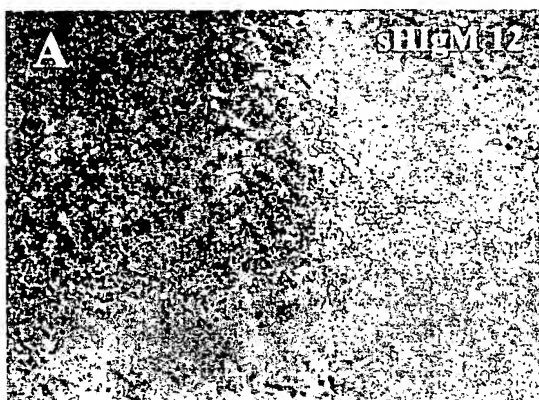


FIG. 20B

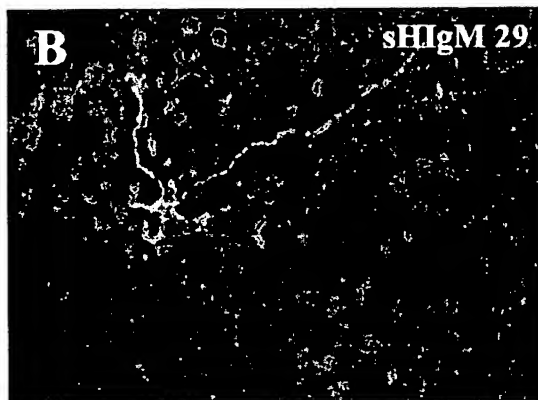


FIG. 20C



FIG. 20D

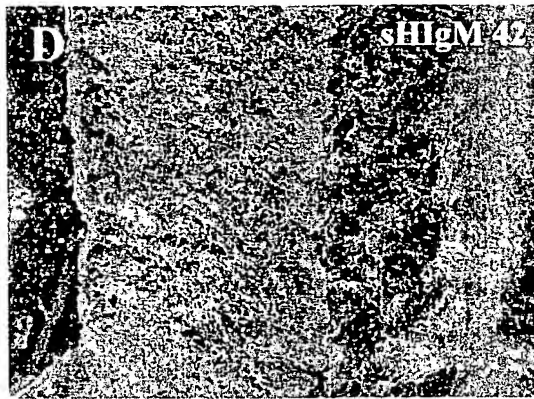


FIG. 20E



FIG. 20F



FIG. 21A

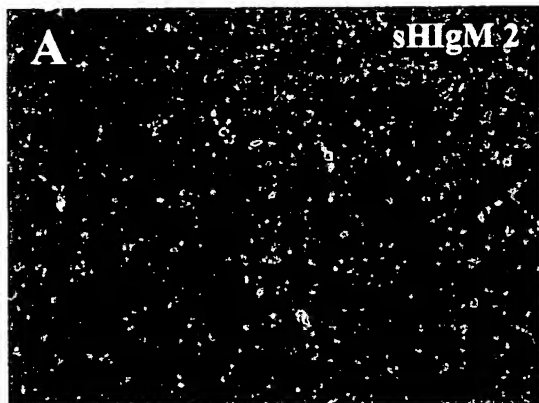


FIG. 21B



FIG. 21C

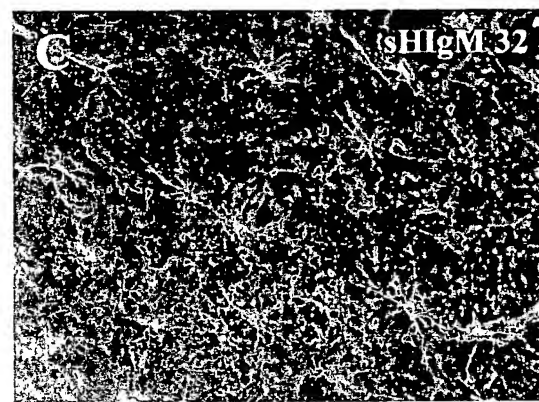


FIG. 21D

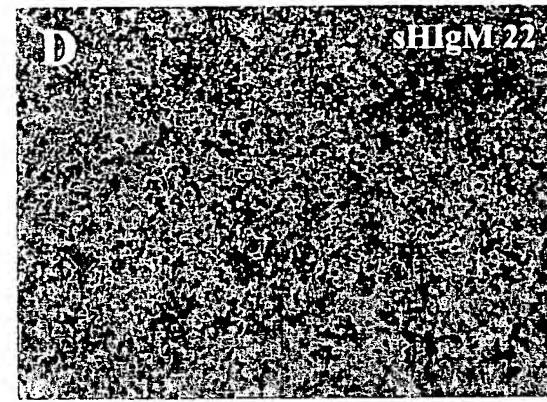


FIG. 21E



FIG. 22A

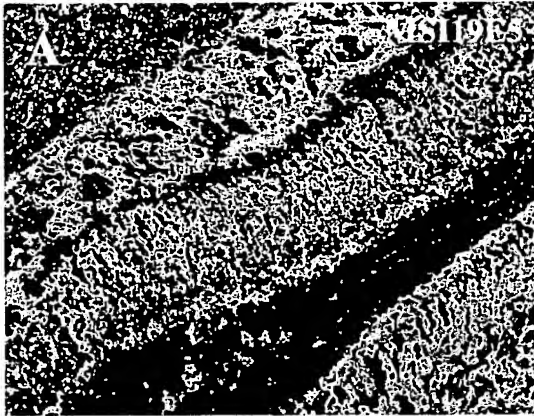


FIG. 22B

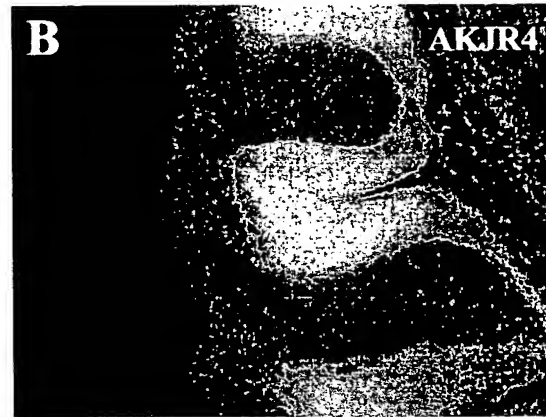


FIG. 22C

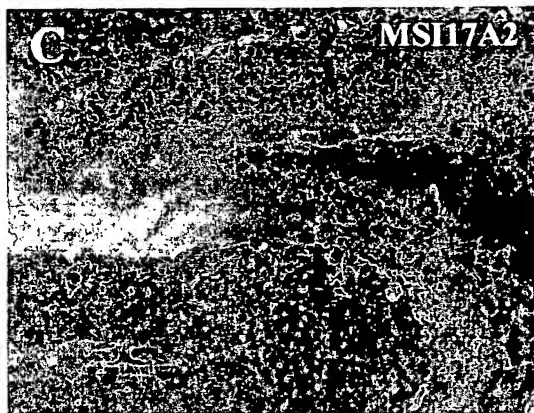


FIG. 22D

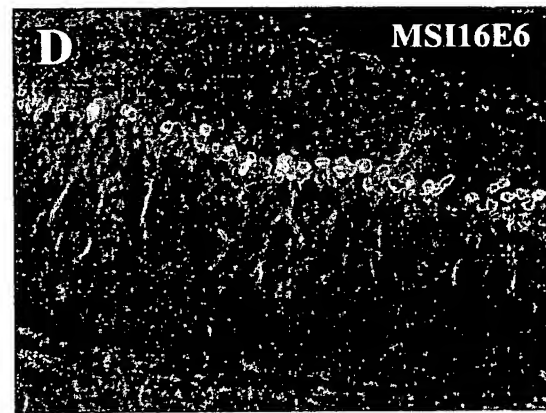


FIG. 22E

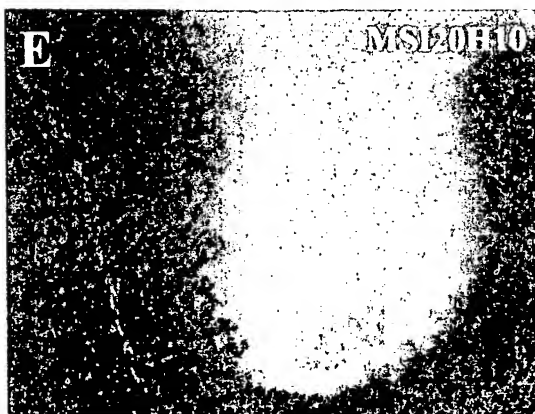


FIG. 22F



FIG. 23B

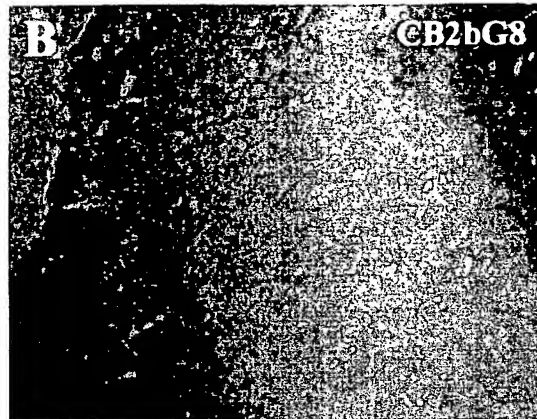


FIG. 23D

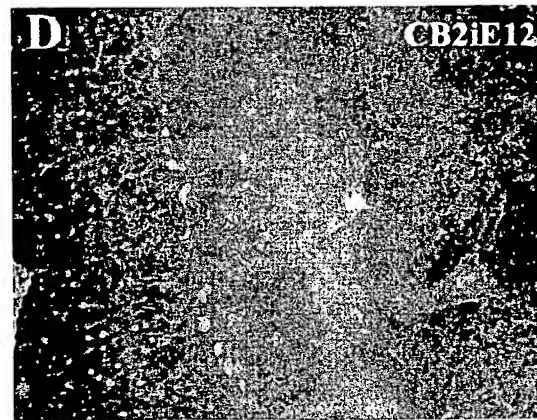


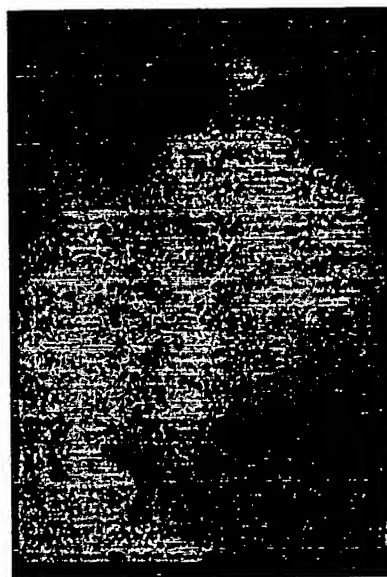
FIG. 23F



FIG. 24B



Polyclonal hIgM

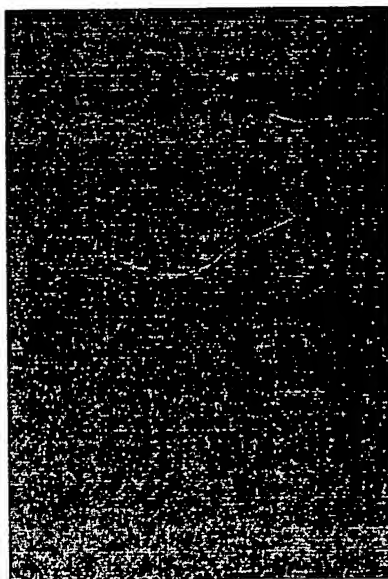


MBP+ OL

FIG. 24E



Polyclonal hlgG



sHlgM 1



sHlgM 2

FIG. 25A



FIG. 25B

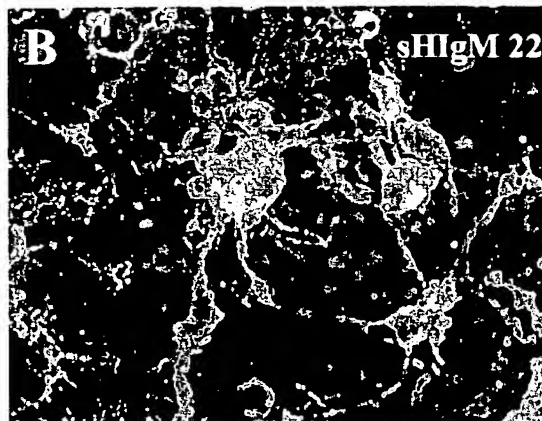


FIG. 25C

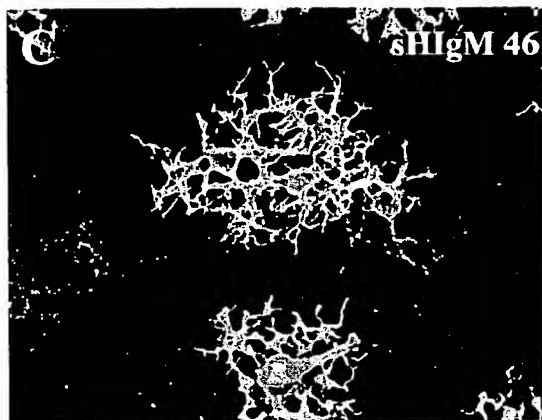


FIG. 25D

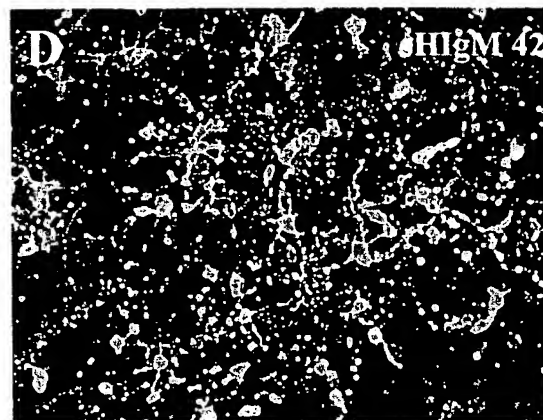


FIG. 25E

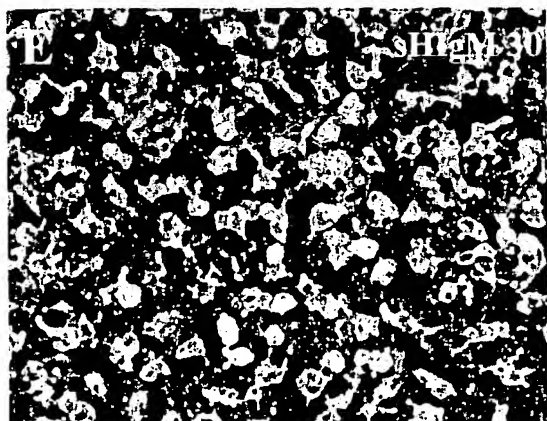
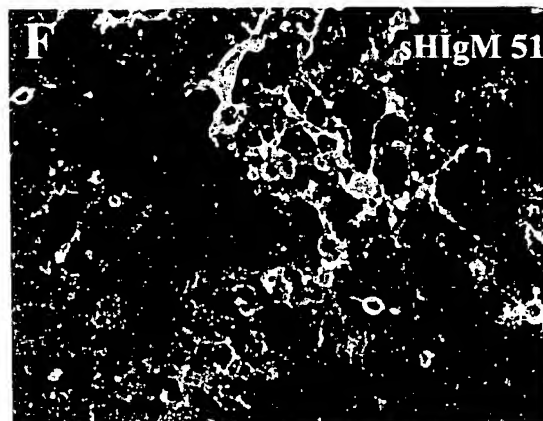


FIG. 25F



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FIG. 26A

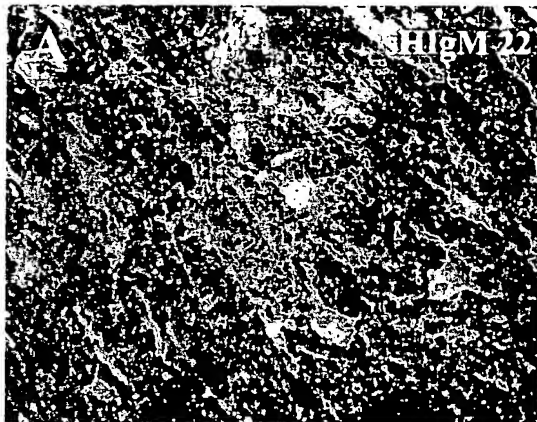


FIG. 26B

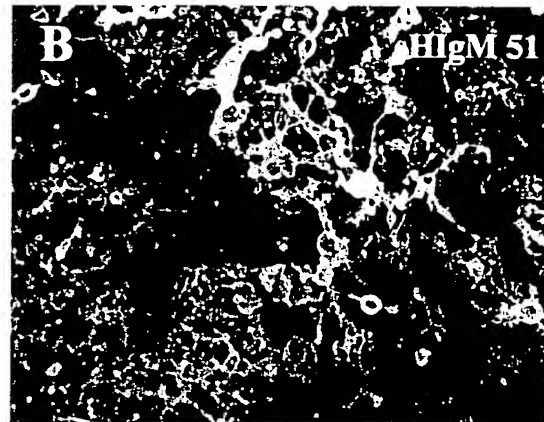


FIG. 26C

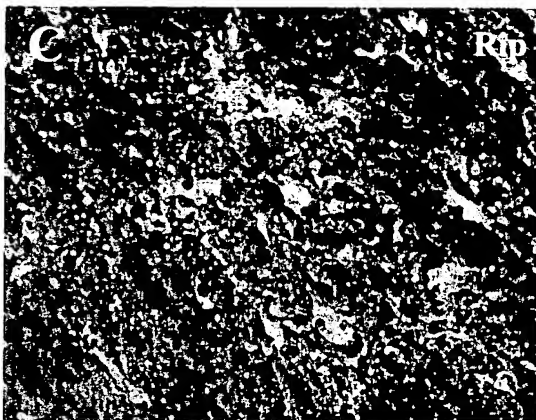


FIG. 26D

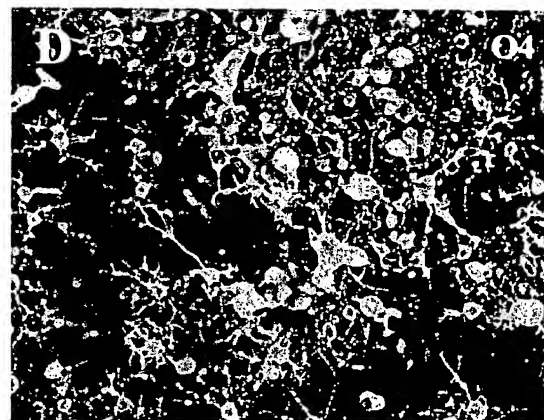


FIG. 26E

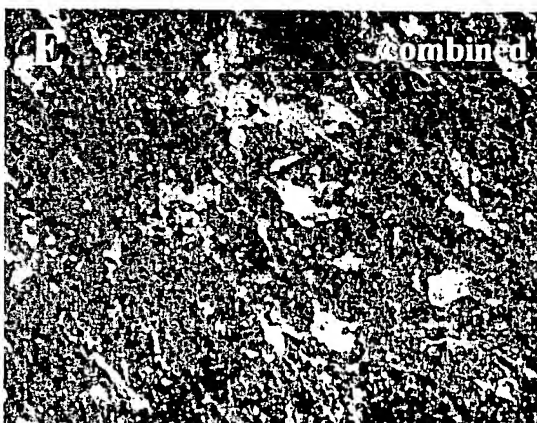
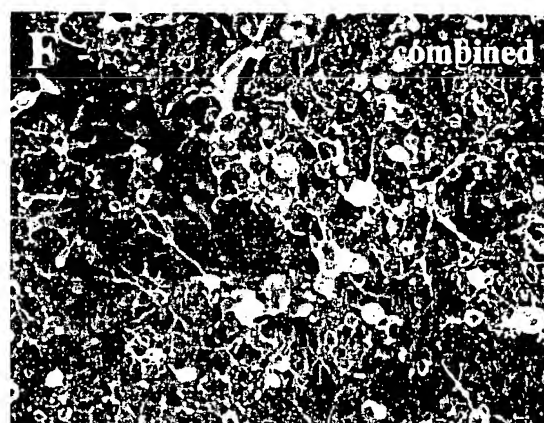


FIG. 26F



09/25/02

FIG. 27A



FIG. 27B

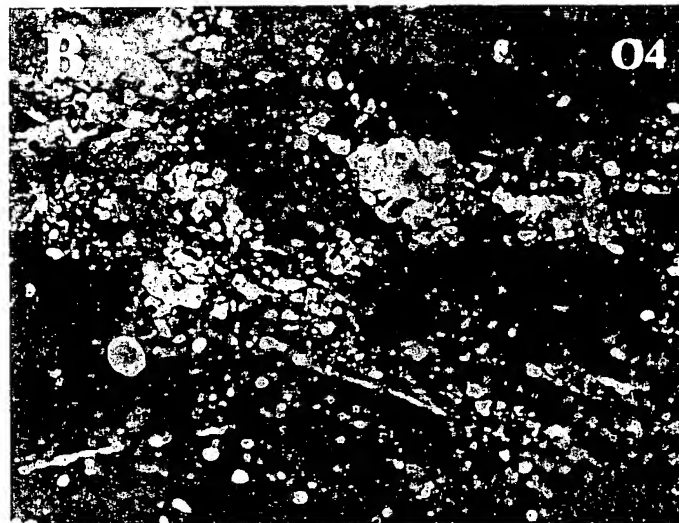


FIG. 27C

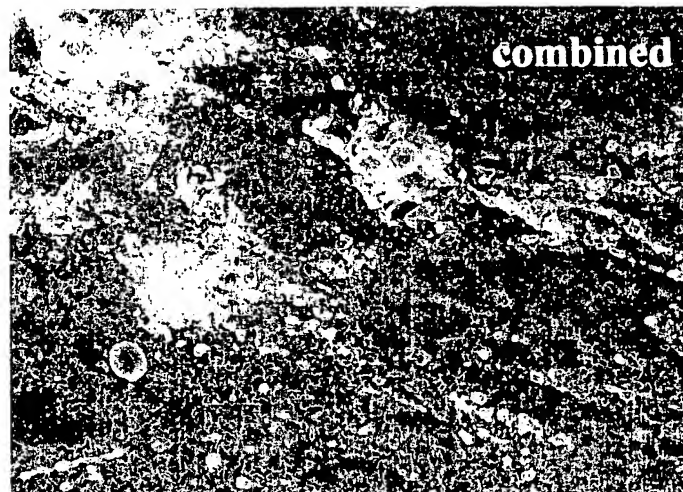




FIG. 29
ebvHlgMs Characterized by Binding to SCH via ELISA

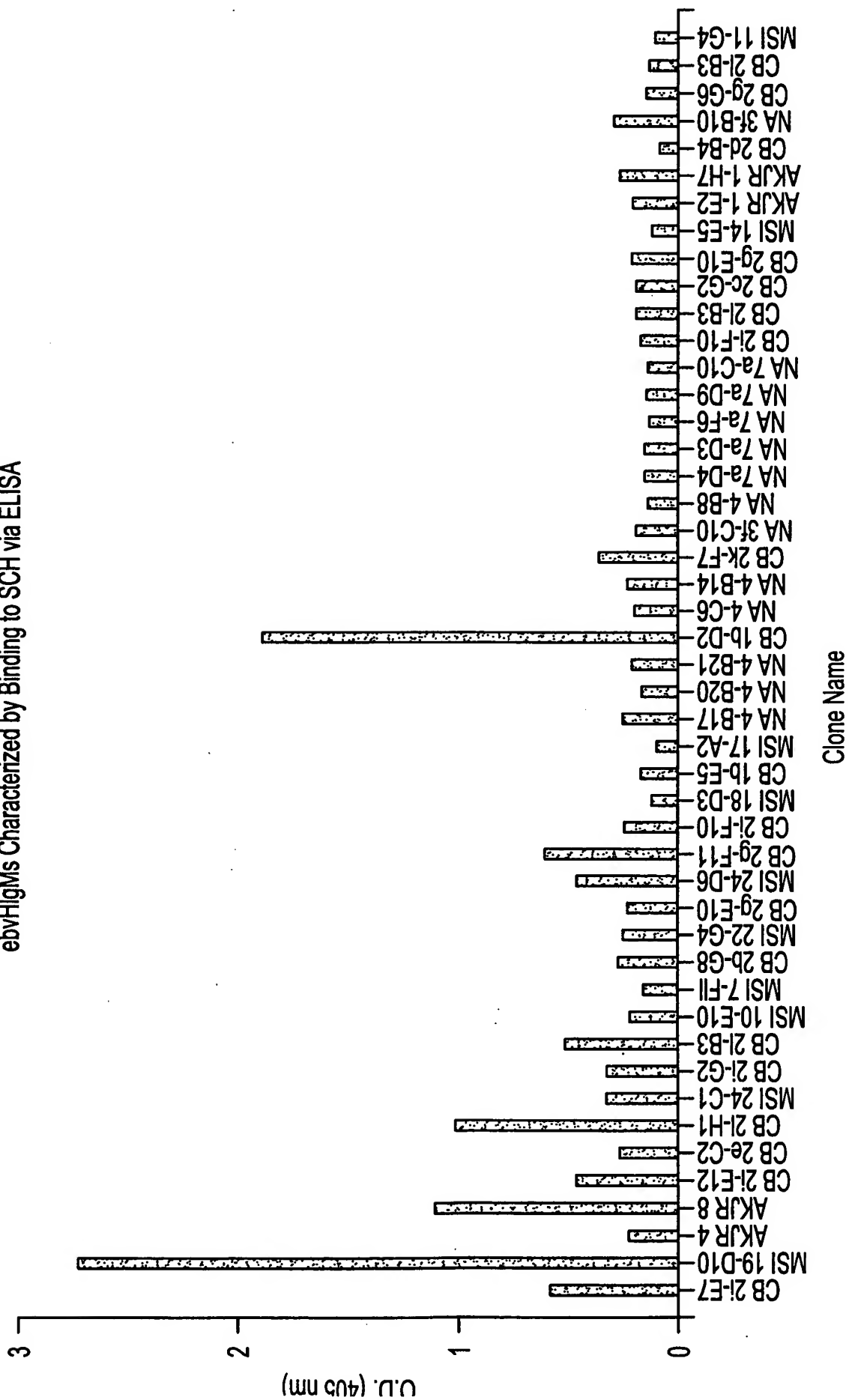


FIG. 30A

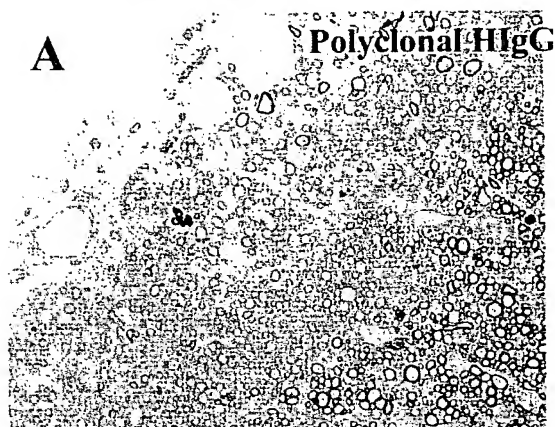


FIG. 30B

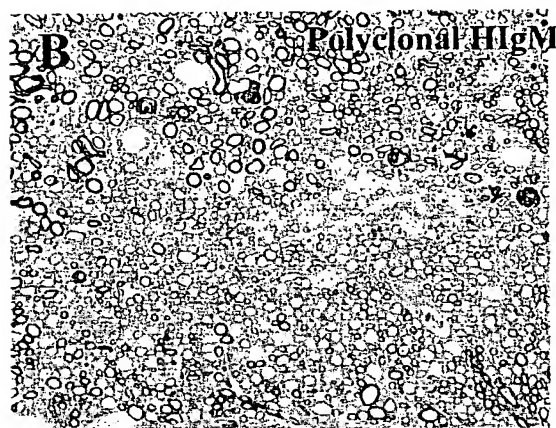


FIG. 30C

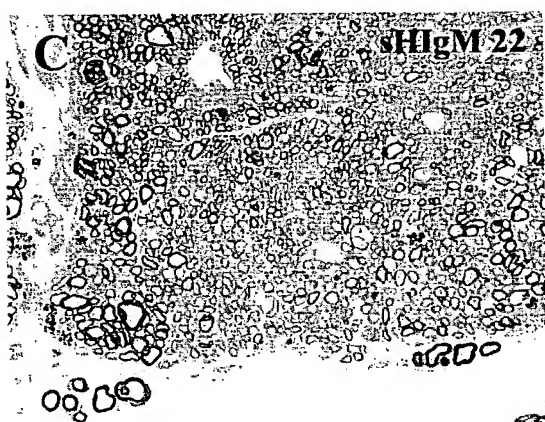


FIG. 30D



FIG. 30E

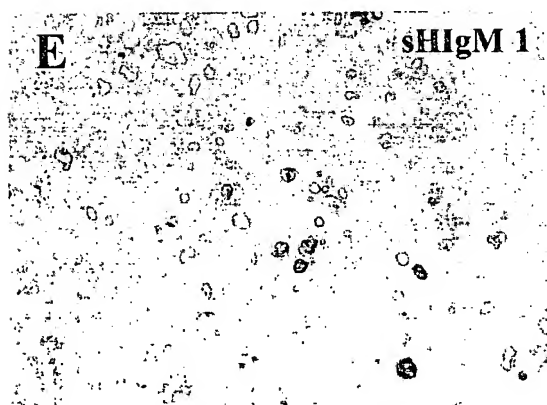


FIG. 30F

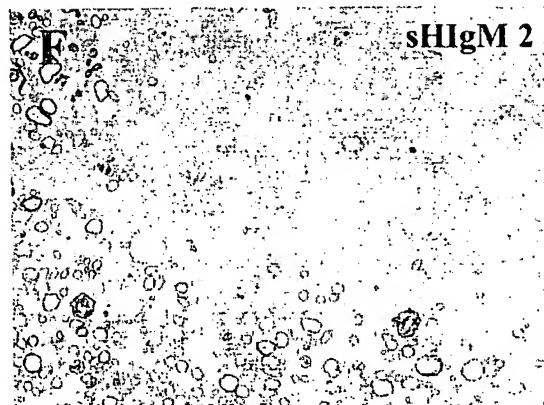


FIG. 31A

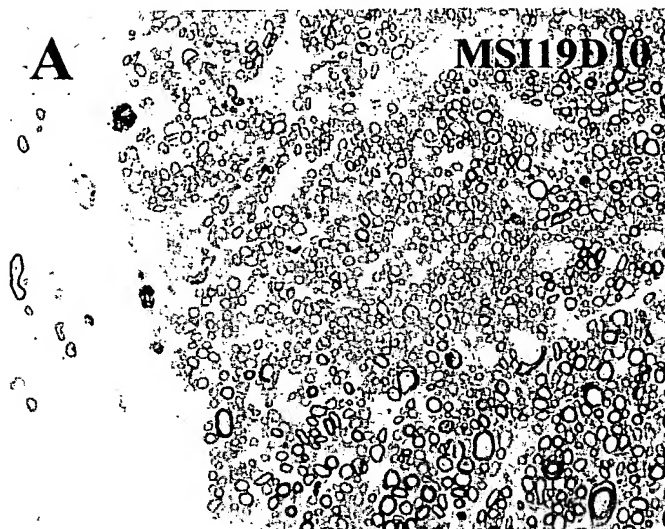


FIG. 31B

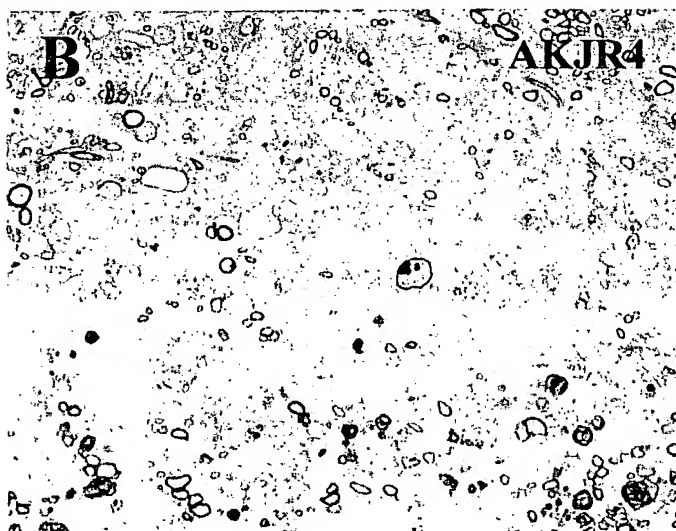
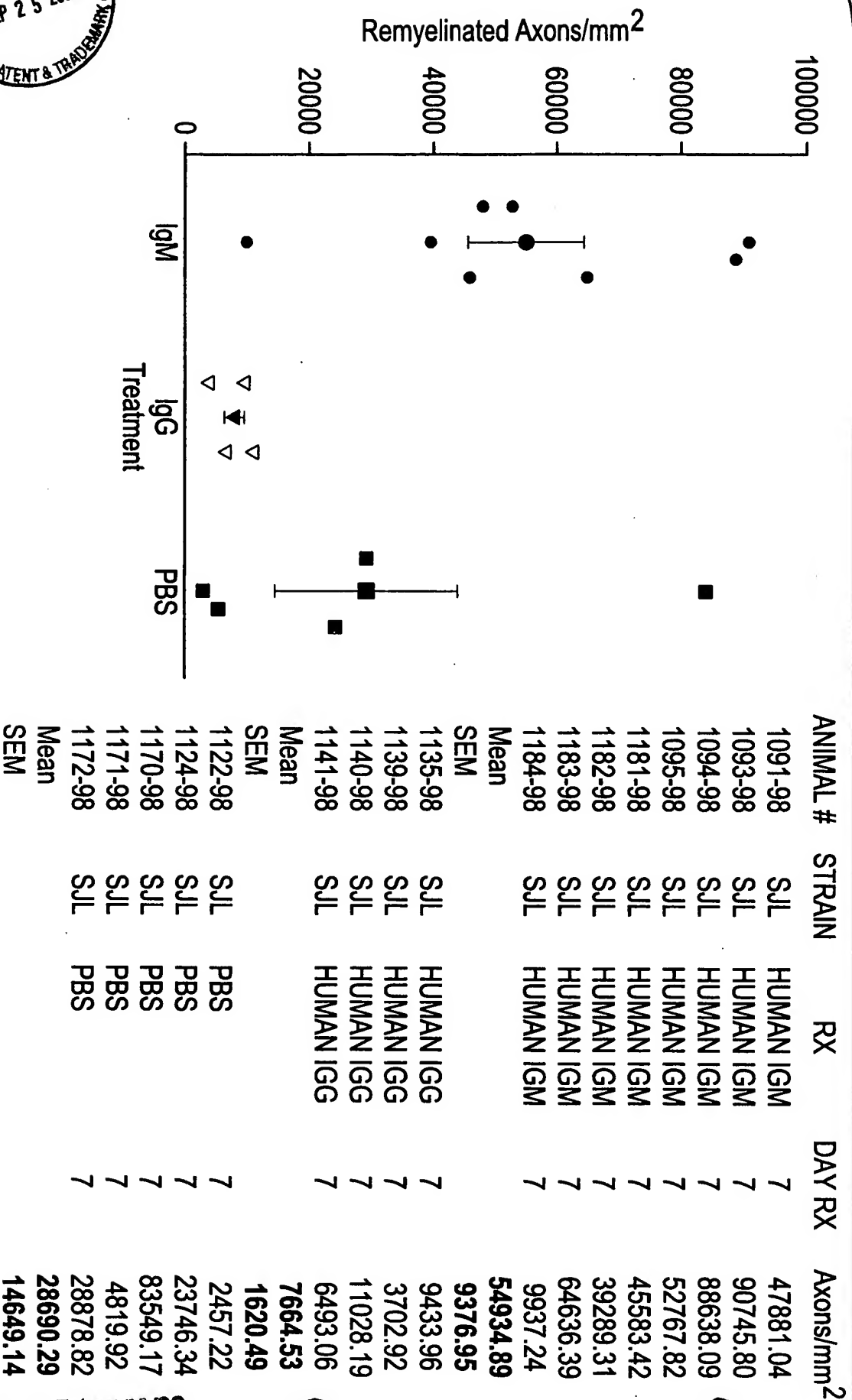


FIG. 32

Lysolecithin Experiment 21 Day Experiment



SCANNED #

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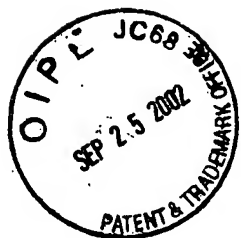
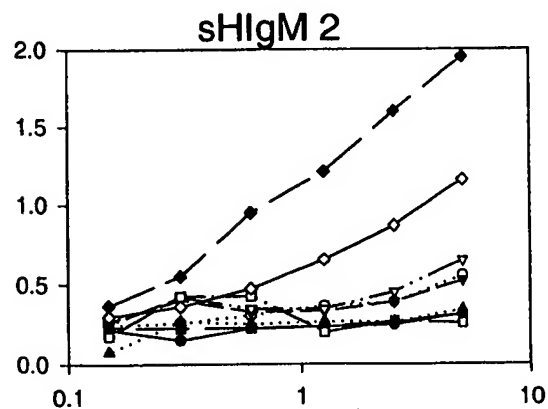
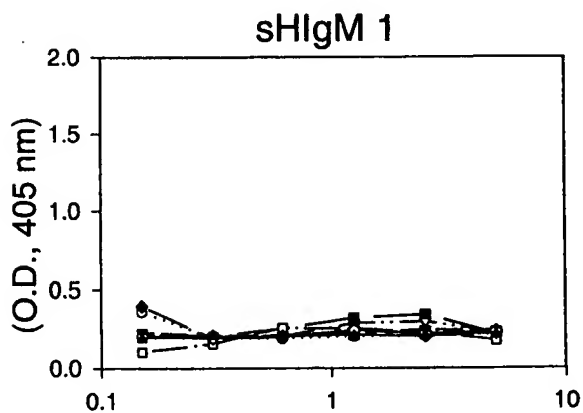
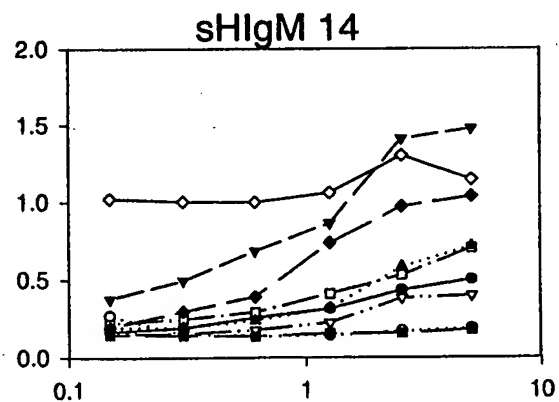
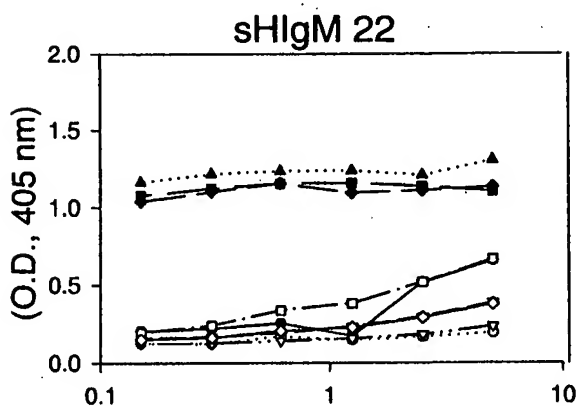
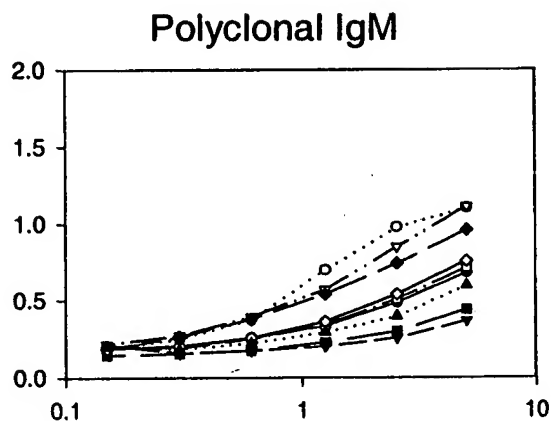
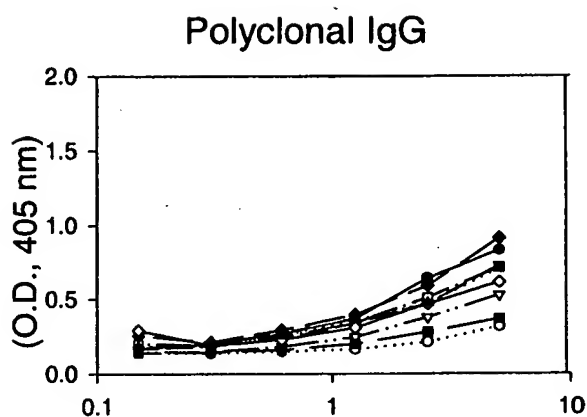


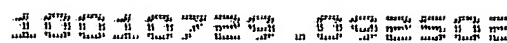
FIG. 33

Hapten Elisa

- KLH
- TMA
- ARS
- PC
- TNP
- PhoX
- NP
- FITC
- DNP



Log Antibody concentration ($\mu\text{g/ml}$)



Protein Elisa

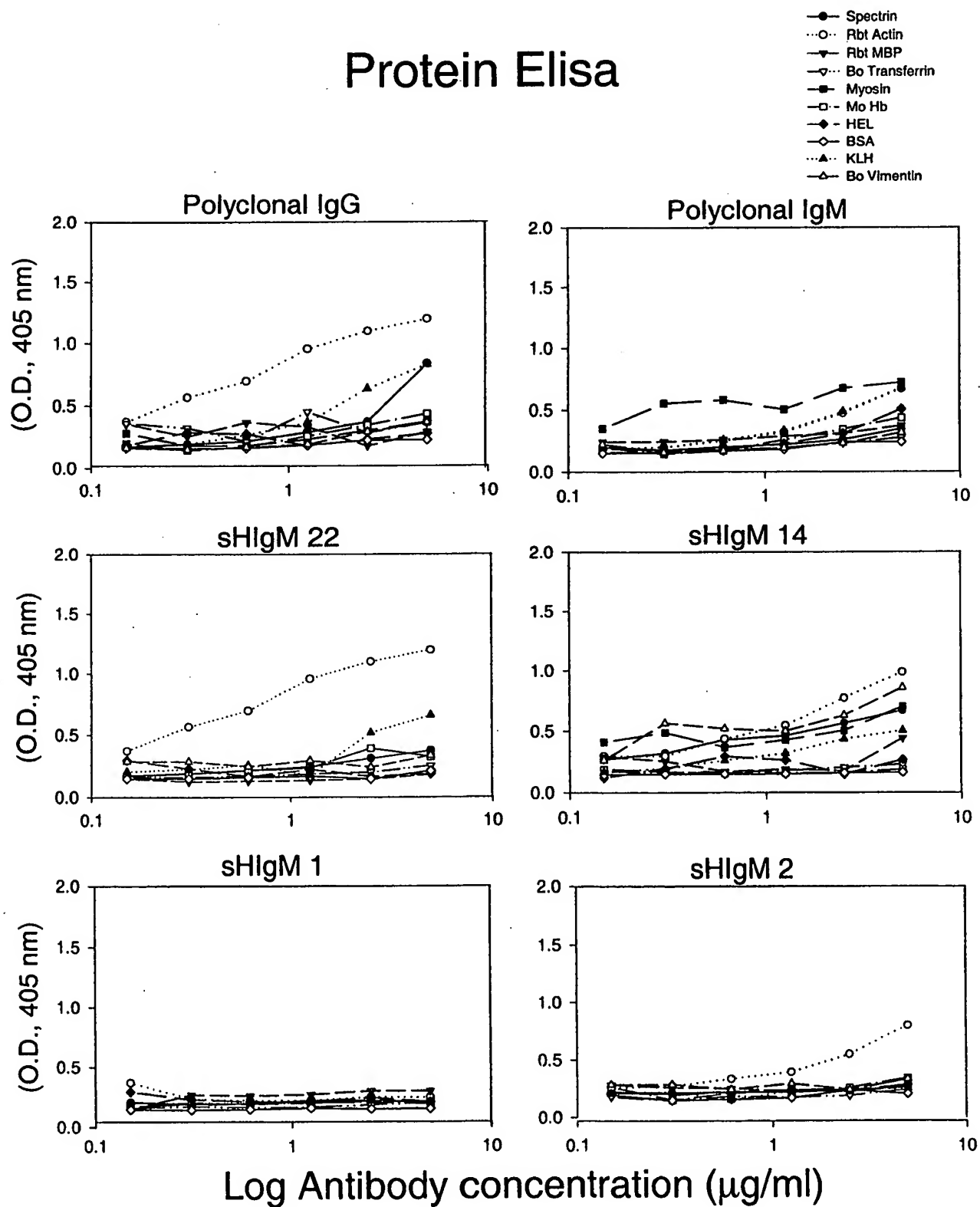




FIG. 35

/FR1-----
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
O V O L V E S G G G G V V O P G
CAG GTG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG
Clone A sH-IgM.22 VH G
Clone B sH-IgM.22 VH

16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
R S L R L S C A A S G F T F S
AGG TCC CTG AGA CTC TCC TGT GCA GCC TCT GGA TTC ACC TTC AGT

/CDR1-----/FR2-----
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45
S S G M H W V R Q A P G K G L
AGC TAT GGC ATG CAC TGG GTC CGC CAG GCT CCA GGC AAG GGG CTG
C A
C

/CDR2-----
46 47 48 49 50 51 52 52A 53 54 55 56 57 58 59
E W V A V(I) I S Y D G S R K Y Y
GAG TGG GTG GCA GTT ATA TCA TAT GAT GGA AGT AAT AAA TAC TAT
T GG
A C T GG

/FR3-----
60 61 62 63 64 65 66 67 68 69 70 71 72 73 74
A D S V K G R F T I S R D N S
GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA GAC AAT TCC
C C
C

75 76 77 78 79 80 81 82 82A 82B 82C 83 84 85 86
K N T L Y L O M N S L T A D(E) D
AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GCT GAG GAC
T CG C
T C

/CDR3-----
87 88 89 90 91 92 93 94 95 96 97 98 99 100 100A
T A V Y Y C A K G V T G S P T
ACG GCT GTG TAT TAC TGT GCG AAA GAG GTG ACT GCT ATT CCC TAC
T GA G G G ACG
GA G G G ACG

/FR4-----
100B 101 102 103 104 105 106 107 108 109 110 111 112 113
L D Y W G O G T L V T V S S
TTT GAC TAC TGG GGC CAG GGA ACC CTG GTC ACC GTC TCC TCA
C G
C G



FIG. 36

```

/FR1-----
1   2   3   4   5   6   7   8   9   11  12  13  14  15  16
O   S   V   L   T   O   P   P   S   V   S   A   A   P   G
CAG TCT GTG TTG ACG CAG CCG CCC TCA GTG TCT GCG GCC CCA GGA
Clone I sH-IgM.22 Vλ      G           T           T
Clone II sH-IgM.22 Vλ     G           T           T
-----/CDR1-----
17  18  19  20  21  22  23  24  25  26  27  27A 27B 28  29
O   K   V   T   I   S   C   S   G   S   S   S   N   I   G
CAG AAG GTC ACC ATC TCC TGC TCT GGA AGC AGC TCC AAC ATT GGG
C
C
-----/FR2-----
30  31  32  33  34  35  36  37  38  39  40  41  42  43  44
N   N   F   V   S   W   Y   O   O   L   P   G   T   A   P
AAT AAT TAT GTA TCC TGG TAC CAG CAG CTC CCA GGA ACA GCC CCC
T
T
A
A
-----/CDR2-----/FR3-----
45  46  47  48  49  50  51  52  53  54  55  56  57  58  59
R(K) L   L   I   Y   D   I   T   K   R   P   S   G   I   P
AAA CTC CTC ATT TAT GAC AAT AAT AAG CGA CCC TCA GGG ATT CCT
G
T
T
C
C
-----
60  61  62  63  64  65  66  67  68  69  70  71  72  73  74
D   R   F   S   G   S   K   S   G   T   S   A   T   L   G
GAC CGA TTC TCT GGC TCC AAG TCT GGC ACG TCA GCC ACC CTG GGC
-----/CDR3-----
75  76  77  78  79  80  81  82  83  84  85  86  87  88  89
I   T   G   L   O   T   G   D   E   A   D   Y   Y   C   G(E)
ATC ACC GGA CTC CAG ACT GGG GAC GAG GCC GAT TAT TAC TGC GGA
A
-----/FR4-----
90  91  92  93  94  95  95A 95B 96  97  98  99 100 101 102
T   W   D   S   S   L   S   A   V   V   F   G   G   G   T
ACA TGG GAT AGC AGC CTG ... ..T GTG GTA TTC GGC GGA GGG ACC
AGT GC
AGT GC
G
G
-----/Cλ-----
103 104 105 106 106A107 108 109 110
K   L   T   V   L   G   O   P   K
AAG CTG ACC GTC CTA GGT CAG CCC AAG

```

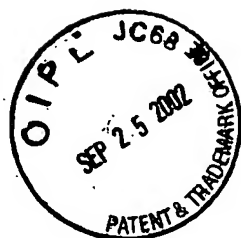


FIG. 37

Sequence of MSI 19-D10 Vh

FR1-----
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG
Q V Q L Q E S G P G L V K P S E

-----/CDR1
17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
ACC CTG TCC CTC ACC TGC ACT GTC TCT GGT GGC TCC ATC AGT AGT
T L S L T C T V S G G S I S S

-----/FR2-----
32 33 34 35 36 37 38 39 40 41 42 43 44 45 46
TAC TAC TGG AGC TGG ATC CGG CAG CCC CCA GGG AAG GGA CTG GAG
Y Y W S W I R Q P P G K G L E

-----/CDR2-----
47 48 49 50 51 52 53 54 55 56 57 58 59 60 61
TGG ATT GGG TAT ATC TAT TAC AGT GGG AGC ACC AAC TAC AAC CCC
W I G Y I Y Y S G S T N Y N P

-----/FR3-----
62 63 64 65 66 67 68 69 70 71 72 73 74 75 76
TCC CTC AAG AGT CGA GTC ACC ATA TCA GTA GAC ACG TCC AAG AAC
S L K S R V T I S V D T S K N

77 78 79 80 81 82 82A 82B 82C 83 84 85 86 87 88
CAG TTC TCC CTG AAG CTG AGC TCT GTG ACC GCT GCG GAC ACG GCC
Q F S L K L S S V T A A D T A

-----/CDR3-----
89 90 91 92 93 94 95 96 97 98 99 100 100A 100B 100C
GTG TAT TAC TGT GCG AGG TCG GCA CAG CAG CAG CTG GTA TAC TAC
V Y Y C A R S A Q Q Q L V Y Y

-----/FR4-----/Cμ-
100D 101 102 103 104 105 106 107 108 109 110 111 112 113 114
TTT GAC TAC TGG GGC CAG GGA ACC CTG GTC ACC GTC TCC TCA GGG
F D Y W G Q G T L V T V S S G

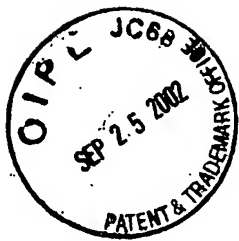


FIG. 39A

Mixed Primary Glia
sH-IgM.22 Ca^{2+} response

- ratio cell #1
- ratio cell #2
- △ sH-IgM.22 ($3\mu\text{g/ml}$)
- ▲ Br-A23187 ($10\mu\text{M}$)

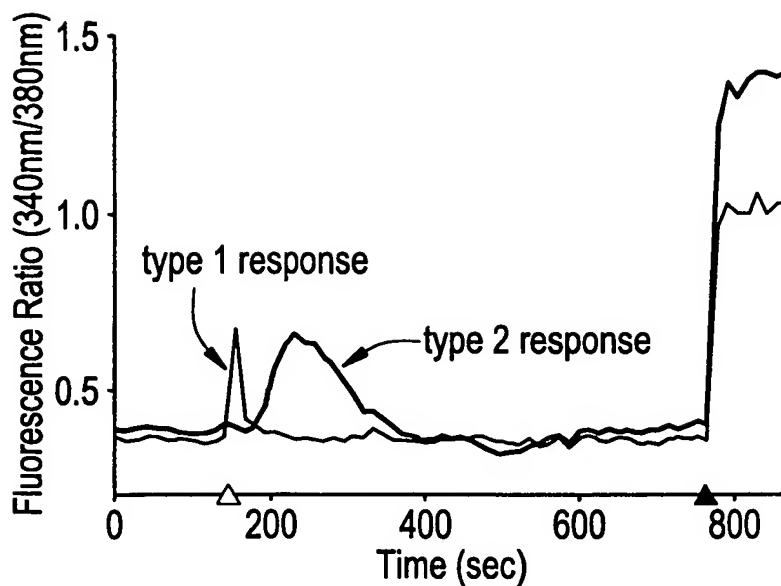


FIG. 39B

Mixed Primary Glia
SCH 94.03 Ca^{2+} response

- ratio cell #1
- ratio cell #2
- △ SCH 94.03 ($3\mu\text{g/ml}$)
- ▲ Br-A23187 ($10\mu\text{M}$)

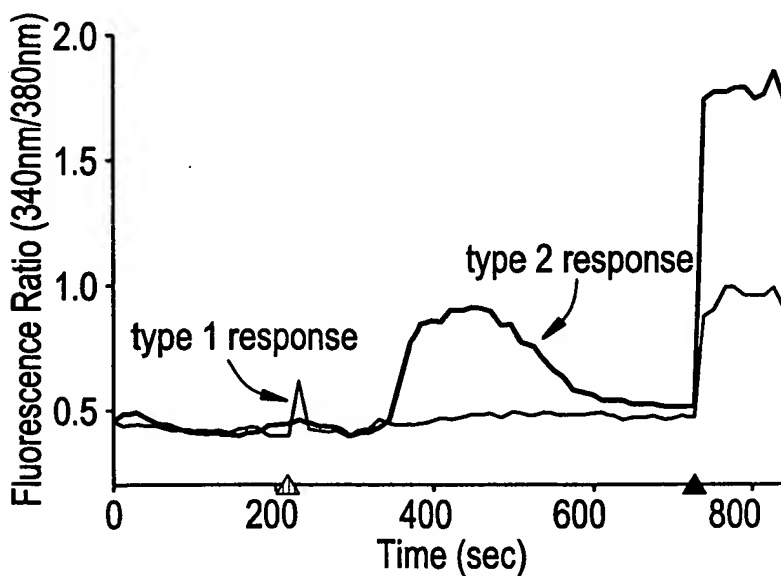


FIG. 39C

Mixed Primary Glia
CH 12/sH-IgM.14 Ca^{2+} response

- ratio cell #1
- ratio cell #2
- △ CH 12 ($3\mu\text{g/ml}$)
- △ sH-IgM.14 ($3\mu\text{g/ml}$)
- ▲ Br-A23187 ($10\mu\text{M}$)

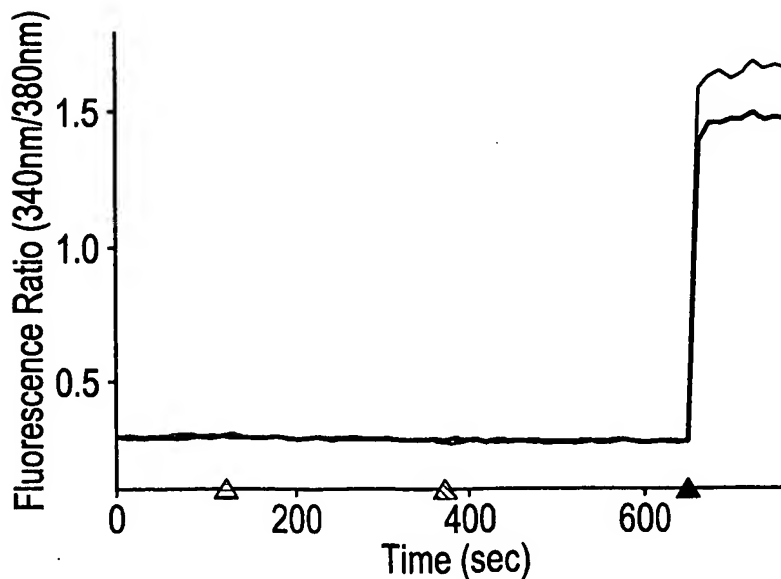


FIG. 40A

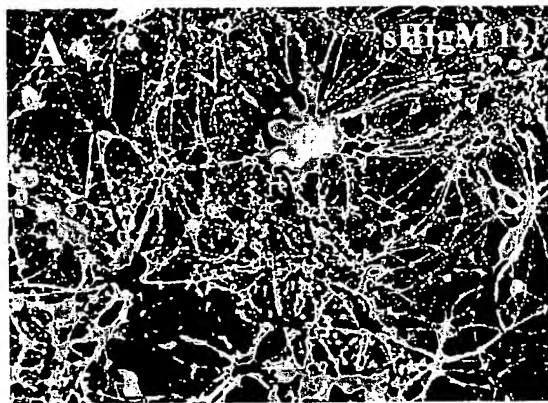


FIG. 40B



[illegible]

jc685 U.S. PTO
09/25/02

FIG. 41

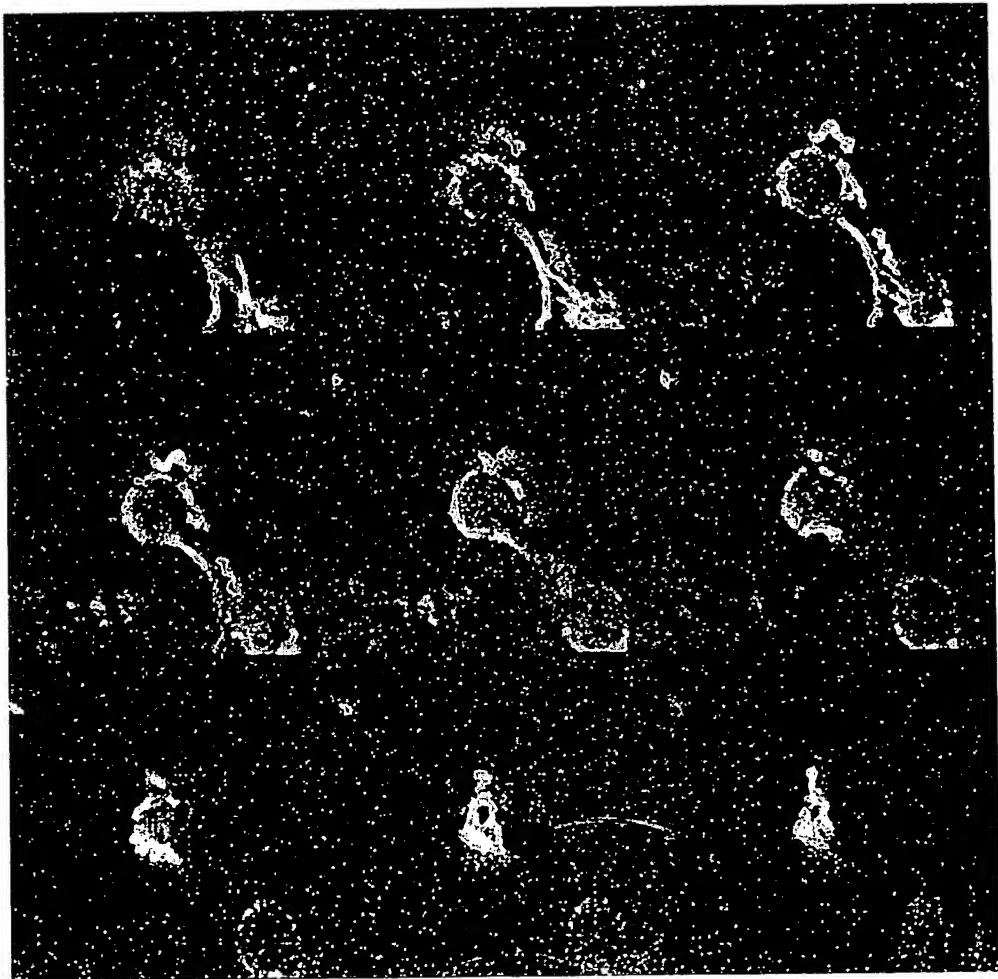


FIG. 42A

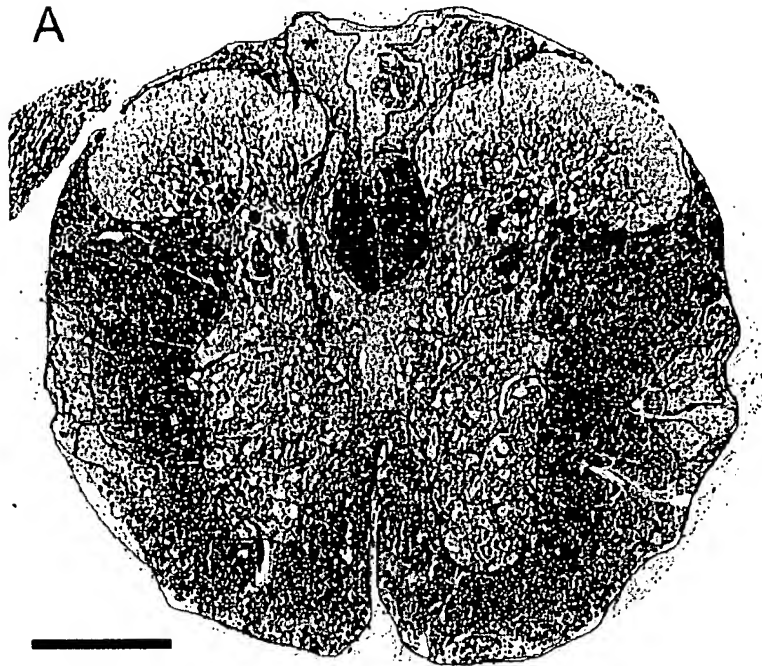
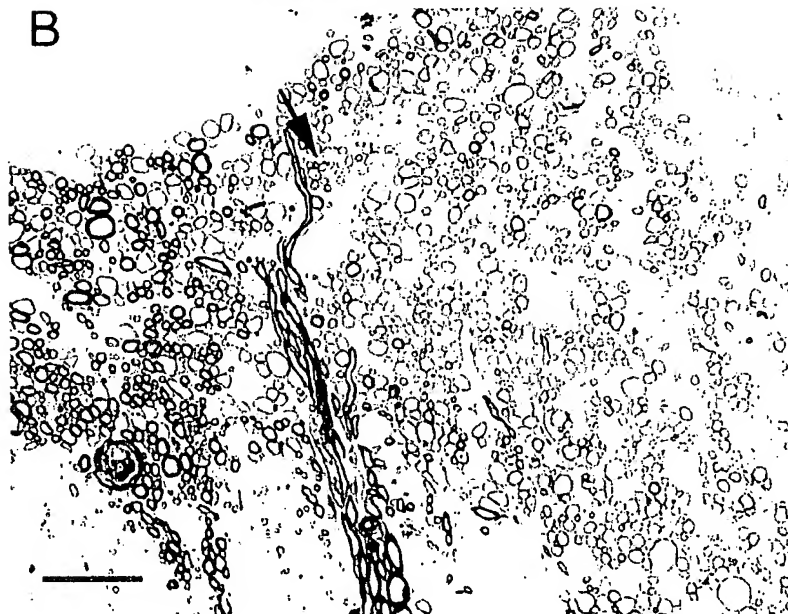


FIG. 42B



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jc685 U.S. PRO

FIG. 43A



FIG. 43B

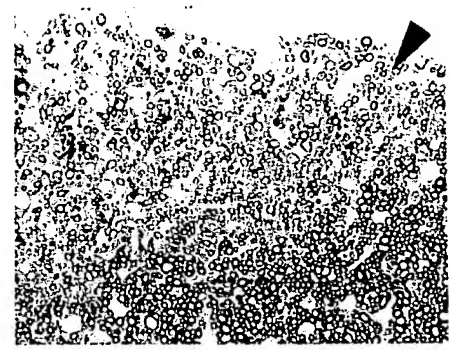


FIG. 43C

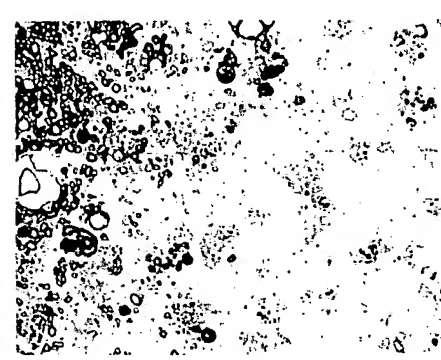


FIG. 43D

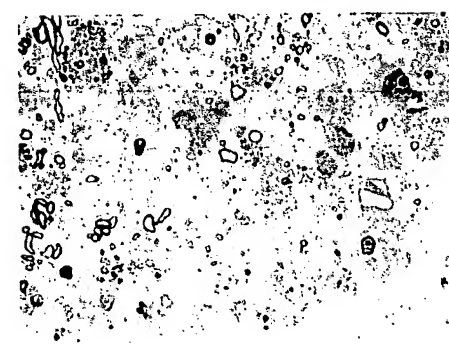


FIG. 43E

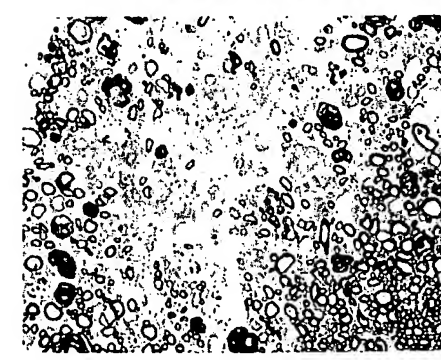


FIG. 43F



FIG. 43G

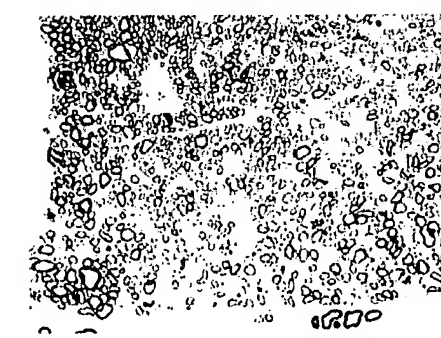


FIG. 43H

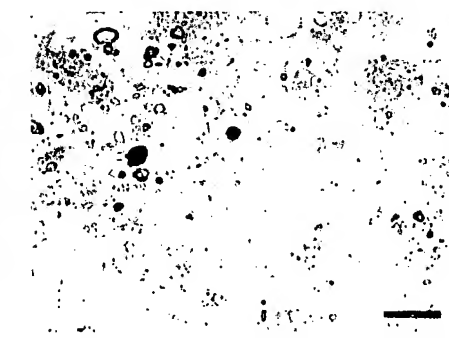


FIG. 44A

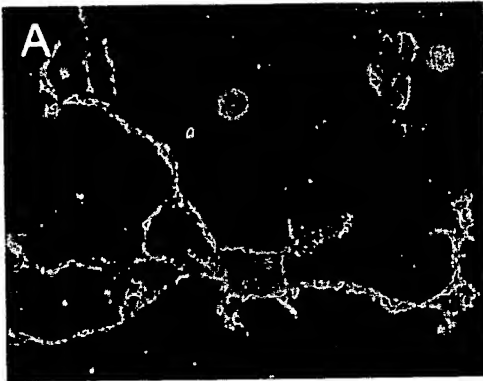


FIG. 44B

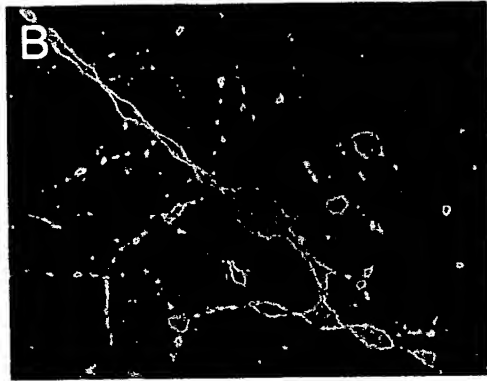


FIG. 44C

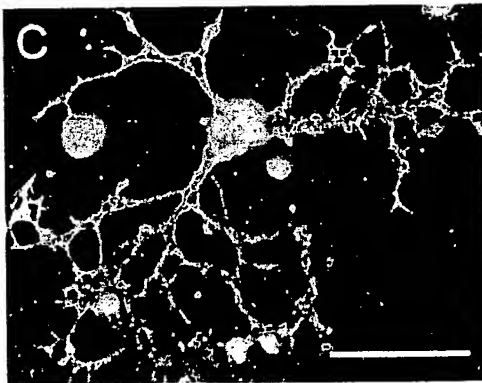


FIG. 44D

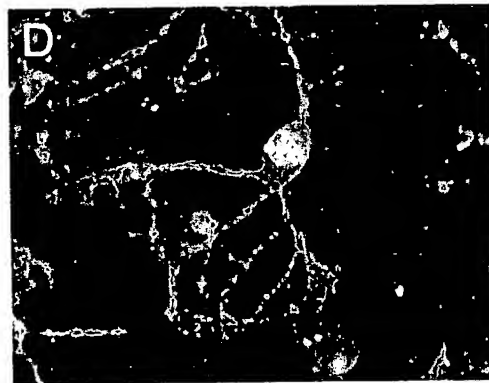


FIG. 45

Translation of CB2b-G8 V_H:

```

<----- F R 1 - I M G T -----
1           5           10           15           20
... .. x A V V Q P G R S L R L S
... .. .AG ... GCC GTG GTC CAG CCT GGG AGG TCC CTG AGA CTC TCC

----->
                CDR1 - IMGT
25           30           35           40
C A A S G F I F S S Y G M H W V R Q
TGT GCA GCG TCT GGA TTC ATT TTC AGT AGC TAT GGC ... .. ATG CAC TGG GTC CGC CAG

F R 2 - I M G T ----->
45           50           55           60           65
V P G K G L E W V A V I W Y D G S D K Y
GTT CCA GGC AAG GGG CTG GAG TGG GTG GCA GTT ATA TGG TAT GAT GGA AGT GAT AAA ... .. TAC

----->
                F R 3 - I M G T -----
70           75           80           85
Y V D S V K G R F T I S R D N S K N T L Y
TAT GTA GAC TCC GTG AAG ... GGC CGA TTC ACC ATC TCC AGA GAC AAT TCT AAA AAC ACG CTC TAT

----->
90           95           100           105           110
L Q M N S L R A E D T A V Y Y C A R D R S S
CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC ACG GCT GTG TAT TAC TGT GCG AGA GAT CGC AGC AGT

CDR3 - IMGT
115           120           125
G W Y W S C D S W G Q G T L V I V S S
GGC TGG TAC TGG TCC TGC GAC TCC TGG GGC CAG GGA ACC CTG GTC ATT GTC TCC TCA

```




FIG. 46

Translation of CB2b-G8 V_λ

<----- F R 1 - I M G T ----->

1 5 10 15 20
... .TT XGC CTC ... CTG TCT GGG TCT CCT GGA CAG TCG ATC ACC ATC TCC

-----> CDR1 - IMGT <----->

25 30 35 40
C T G T S S D V G G Y N Y V S W Y Q Q
CTG ACT GGA ACC AGC AGT GAC GTT GGT GGT TAT AAC TAT ... GTC TCC TGG TAC CAA CAG

F R 2 - I M G T -----> CDR2 - IMGT <----->

45 50 55 60 65
H P G K A P K L M I Y D V S ... D
CAC CCA GGC AAA GCC CCC AAA CTC ATG ATT TAT GAT GTC AGT ... GAT

-----> F R 3 - I M G T ----->

70 75 80 85
R P S G V S N R F S G S K S G N T A S
CGG CCC TCA GGG GTT TCT ... AAT CGC TTC TCT GGC TCC AAG ... TCT GGC AAC ACG GCC TCC

-----> CDR3 - IMGT

90 95 100 105 110
L T I S G L Q A E D E A D Y Y C S S Y T S S
CTG ACC ATC TCT GGG CTC CAG GCT GAG GAC GAG GCT GAT TAT TAC TGC AGC TCA TAT ACA AGC AGC

115 120 125
S S V V F G G G T K L T V L G Q P K A A P S
AGC TCT GTG GTA TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA GGT CAG CCC AAG GCT GCC CCC TCG

V T L F P P P x
GTC ACT CTG TTC CCG CCT CCA AXG G

FIG. 47A

DHFR amplification of 94.03k

4	5
0.2	51.2
0.2	51.2
Neg	Pos



FIG. 47B

Clone #4 Kappa Chain Elisa

□ 0.2 ug/ml methotrexate
■ 51.2 ug/ml methotrexate

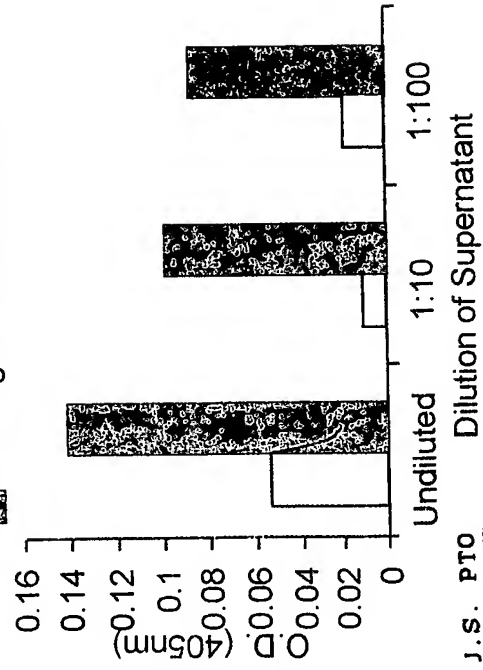


FIG. 47C

Clone #5 Kappa Chain Elisa

□ 0.2 ug/ml methotrexate
■ 51.2 ug/ml methotrexate

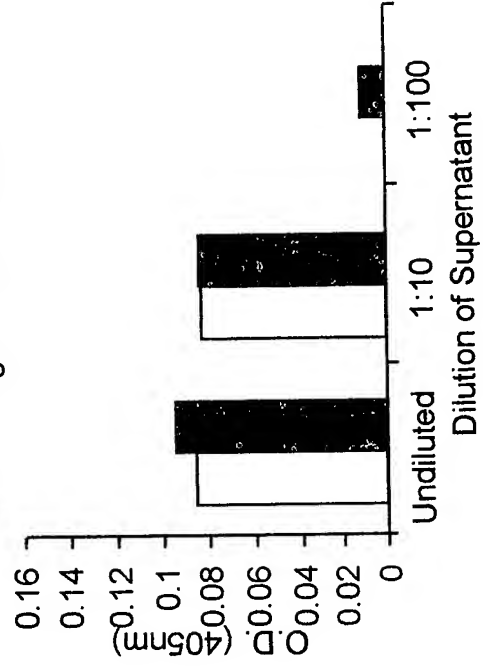
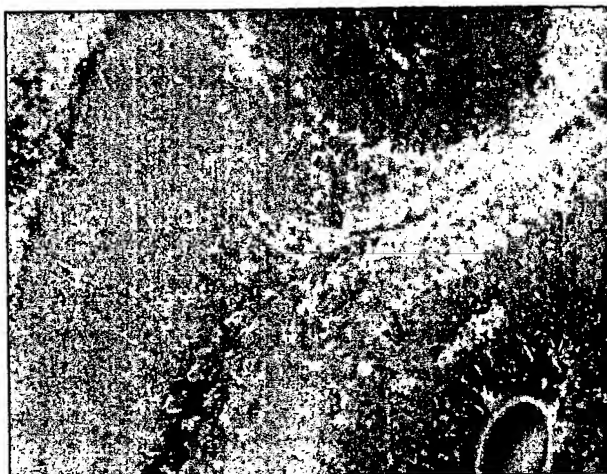


FIG. 49A



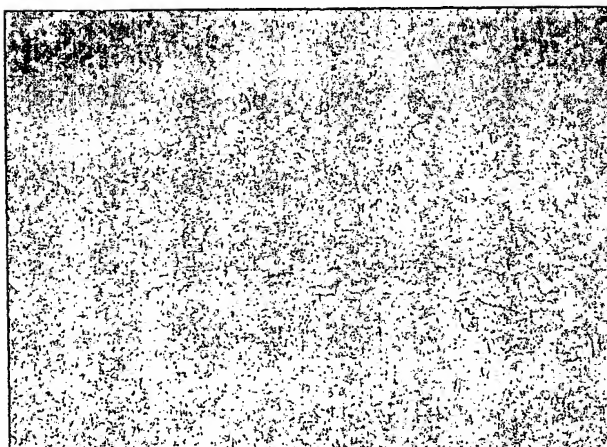
Mouse 94.03

FIG. 49B



Humanized 94.03
clone 1

FIG. 49C



Humanized 94.03
clone 2



FIG. 50A

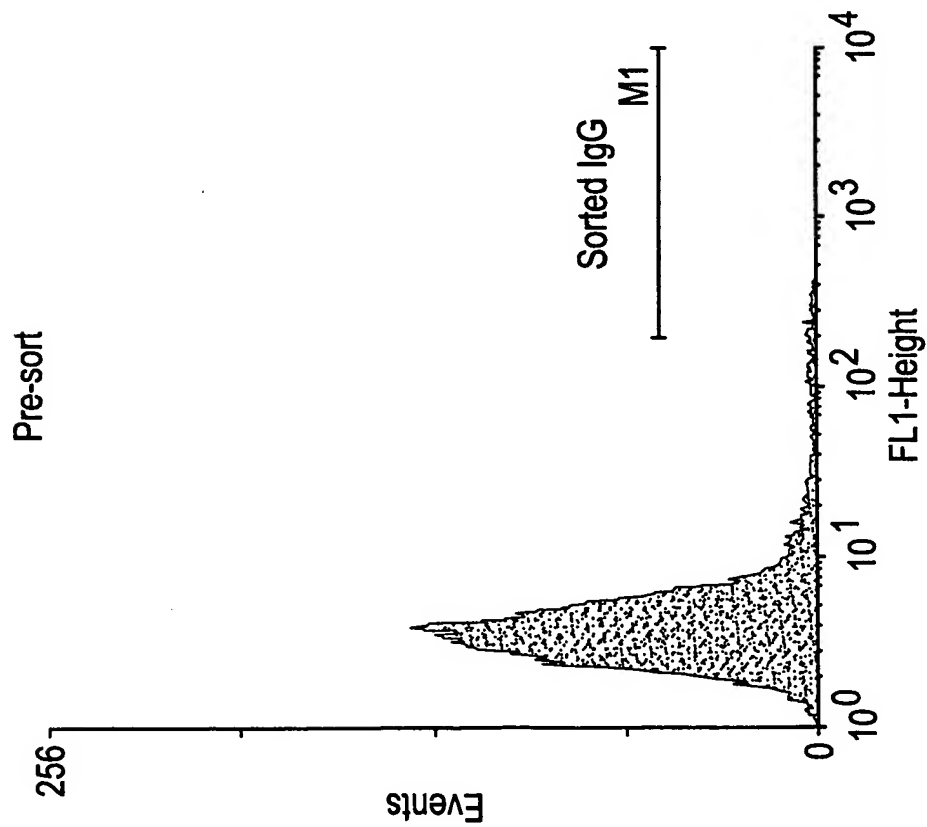


FIG. 50B

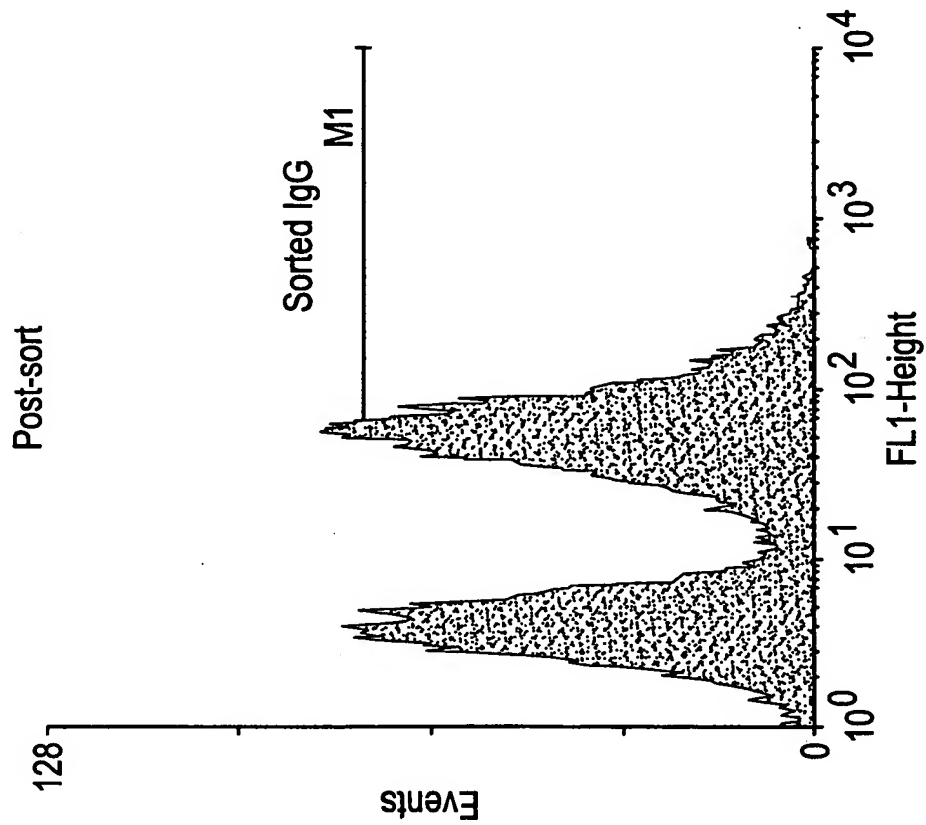




FIG. 51
Sequencing of 94.03 IgG

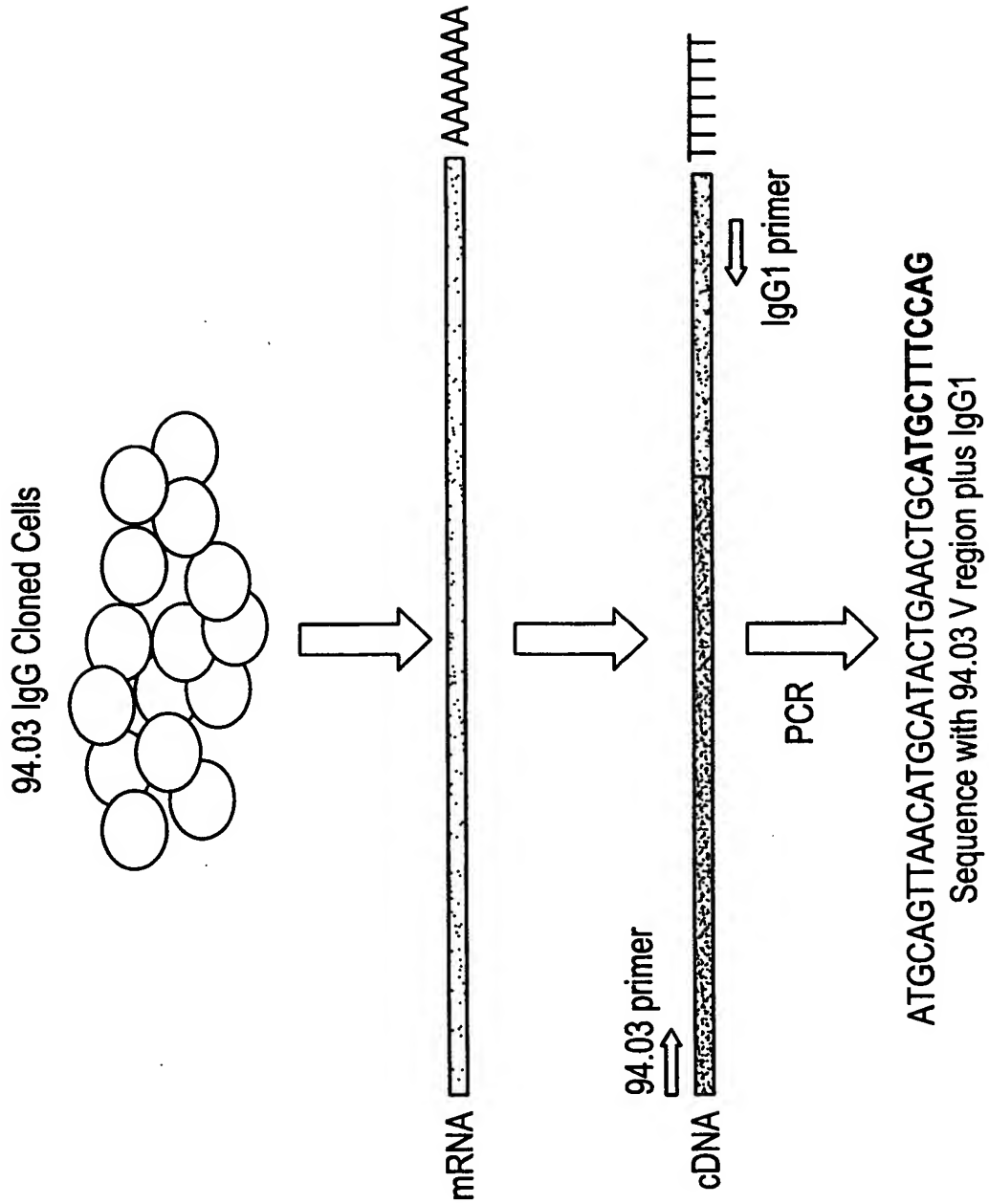




FIG. 52

09 V_R Sequence with translation:

<----- F R 1 - I M G T ----->

1 5 10 15 20
Q D H L Q Q S G P E L V K P G A F V K I S
CAG GAT CAC CTG CAG CAG TCT GGA CCT ...GAG CTG GTG AAG CCT GGG GCT TTT GTG AAG ATA TCC

----->

CDR1 - IMGT

25 30 35 40
C K A S G Y T F T N Y D L N W V R Q
TGC AAG GCT TCT GGT TAC ACC TTC ACA AAC TAC GATCTA AAC TGG GTG AGG CAG

F R 2 - I M G T ----->

CDR2 - IMGT

45 50 55 60 65
R P G Q G L E W I G W I Y P G N D N T K
AGG CCT GGA CAG GGC CTT GAG TGG ATT GGA TGG ATT TAT CCT GGA AAT GAT AAT ACTAAG

----->

F R 3 - I M G T --

70 75 80 85
Y N E K F K G L A S L T A D K S S T T A Y
TAC AAT GAG AAG TTC AAG ...GGC CTG GCC TCA CTG ACT GCA GAC AAG TCC TCC ACC ACA GCC TAC

----->

90 95 100 105 110
L H L S S L T S E S S A V Y F C A R G L P R
TTG CAT CTC AGC AGC CTG ACT TCT GAG AGC TCT GCA GTC TAT TTC TGT GCA AGA GGG TTA CCT AGG

CDR3 - IMGT

115 120
G W Y F D V W G A G T T V T V S S A
GGC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCT



Translation of 09 kappa light chain 1:

FIG. 53

<----- F R 1 - I M G T ----->

1 N I V M T Q S P K S M S 10 15 20
AAC ATT GTA ATG ACC CAA TCT CCC AAA TCC ATG TCC ATG TCA GTA GGA GAG AGG GTC ACC TTG ACC

-----> <-----

25 C K A S E N V T Y 30 CDR1 - IMGT 35 40
TGC AAG GCC AGT GAG AAT GTG GTT ACT TAT ... GTT TCC TGG TAT CAA CAG

F R 2 - I M G T -----> <-----
45 K P E Q S P K L L I Y G A S 55 CDR2 - IMGT 60 65
AAA CCA GAG CAG TCT CCT AAA CTG CTG ATA TAC GGG GCA TCC ... AAC

----- F R 3 - I M G T -----

70 R Y T G V P 75 D R F T G S G 80 S A T D F T
CGG TAC ACT GGG GTC CCC ... GAT CGC TTC ACA GGC AGT GGA ... TCT GCA ACA GAT TTC ACT

-----> <----- CDR3 - IMGT
90 L T I S S V Q A E D L A D Y H C G Q G Y S Y 100 105 110
CTG ACC ATC AGC AGT GTG CAG GCT GAA GAC CTT GCA GAT TAT CAC TGT GGA CAG GGT TAC AGC TAT

115
P Y T F G G
CCG TAC ACG TTC GGA GGG GGG



FIG. 54

translation of 09 kappa light chain 2:

```
<----- F R 1 - I M G T ----->
1 5 10 15 20
D V Q I T Q S P S Y L A A
GAT GTC CAG ATA ACC CAG TCT CCA TCT TAT CTT GCT GCA TTT CCT GGA ACC ATT ACT ATT AAT

----->
25 30 35 40
C R A S K S I S K Y L A W Y Q E
TGT AGG GCA AGT AAG AGC ATT AGT AAA TAT ... TTA GCC TGG TAT CAA GAG

F R 2 - I M G T ----->
45 50 55 60 65
R P G K T N K L L I Y S G S
AGA CCT GGA AAA ACT AAT AAG CTT ATC TAC TCT GGA TCC ... ACT

----- F R 3 - I M G T -----
70 75 80 85
L Q S G I P S R F S G S G
TTG CAA TCT GGA ATT CCA ... TCA AGG TTC AGT GGC AGT GGA ... TCT GGT ACA GAT TTC ACT

----->
90 95 100 105 110
L T I S S L E P E D F A M Y Y C Q Q H N E Y
CTC ACC ATC AGT AGC CTG GAG CCT GAA GAT TTT GCA ATG TAT TAC TGT CAA CAG CAT AAT GAA TAC

----->
115
P Y T F G G G
CCG TAT ACG TTC GGA GGG GGG
```

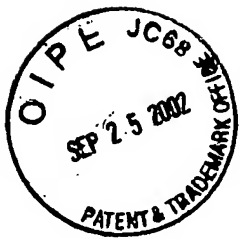



FIG. 55

Translation of AKJR 4 Heavy Chain:

<----- F R 1 - I M G T ----->

1 5 10 15 20
E V Q L L E S G G G L V Q P G G S L R L S
GAG GTG CAA CTA TTG GAA TCT GGG GGA ... GGC TTG GTA CAG CCT GGG GGG TCC CTG AGA CTC TCC

<----->

25 30 35 40
C A A S G F S F I D Y A M S W V R Q
TGT GCA GCC TCT GGA TTC AGC TTT ATC GAC TAT GCC ... ATG AGC TGG GTC CGC CAG

F R 2 - I M G T ----->

45 50 55 60 65
A P G K G L E W V S L S G D S G S Y
GCT CCA GGG AAG GGA CTG GAG TGG GTC TCA AGT CTT AGT GGT GAT AGT TCA ... TAT

----- F R 3 - I M G T ----->

70 75 80 85
Y A D S V K G R F T I S R D N S K S T V F
TAT GCA GAC TCC GTG AAG ... GGC CGA TTC ACC ATC TCC AGA GAC AAT TCC AAG AGC ACG GTG TTT

<----->

90 95 100 105 110
L Q L S S L R A E D T A I Y Y C A Q E T G P
CTG CAA CTG AGC AGC CTG AGA GCC GAG GAC ACC ATA TAT TAT TGT GCG CAG GAG ACC GGT CCC

----- CDR3 - IMGT ----->

115 120 125 130
Q R R W G Q G T L V T V S S G S A S A P T L
CAG CGT CGC TGG GGC CAG GGA ACC CTG GTC ACC GTC TCC TCA GGG AGT GCA TCC GCC CCA ACC CTT

FIG. 56

Translation of AKJR 4 Kappa Light Chain:

```

<----- F R 1 - I M G T -----
1      5      10      15      20
D I Q M T Q S P S T L S A S V G D R V T I T
GAC ATC CAG ATG ACC CAG TCT CCT TCC ACC CTG TCT GCA TCT GTA GGG GAC AGA GTC ACC ATC ACT

----->
25      30      35      40
C R A S Q S I S S W L A W Y Q Q
TGC CGG GCC AGT CAG AGT ATT AGT AGC TGG ... TTG GCC TGG TAT CAG CAG

F R 2 - I M G T ----->
45      50      55      60      65
K P G K A P K L L I Y K A F N
AAA CCA GGG AAA GCC CCT AAA CTC CTG ATC TAT AAG GCG TTT ... AAT

----- F R 3 - I M G T -----
70      75      80      85
L E S G V P S R F R G S G S G T E F T
TTA GAA AGT GGG GTC CCA ... TCA AGG TTC AGA GGC AGT GGC ... TCT GGG ACA GAA TTC ACT

----->
90      95      100      105      110
L T I S S L Q P D D S A T Y Y C Q Q Y S S Y
CTC ACC ATC AGC AGC CTG CAG CCT GAT GAT TCT GCA ACT TAT TAC TGC CAG CAG TAT AGT AGT TAC

----->
115      120      125      130
P L T F G G G T K V D I K R T V A A P S V F
CCC CTC ACT TTC GGC GGA GGG ACC AAG GTG GAC ATT AAA CGA ACT GTG GCT GCA CCA TCT GTC TTC

```





FIG. 57 Translation of CB2i-E12 Heavy Chain:

<----- F R I - I M G T ----->

1 5 10 15 20
x R x x K x E A S V K V S
... .CC AGG ... XAG XAX AXG AAA XCG GAG GCC TCA GTG AAG GTC TCC

<----->

25 30 35 40
C K A S G Y T F T G Y Y M H W V R Q
TGC AAG GCT TCT GGA TAC ACC TTC ACC GGC TAC TAT ... ATG CAC TGG GTG CGA CAG

F R 2 - I M G T -----> CDR1 - IMGT <----->

45 50 55 60 65
A P G Q G L E W M G W I N P N S G G T N
GCC CCT GGA CAA GGG CTT GAG TGG ATG GGA TGG ATC AAC CCT AAC AGT GGT GGC ACA ... AAC

70 75 80 85
Y A Q K F Q G R V T M T R D T S I S T A Y
TAT GCA CAG AAG TTT CAG ... GGC AGG GTC ACC ATG ACC AGG GAC ACG TCC ATC AGC ACA GCC TAC

90 95 100 105 110
M E L S R L R S D D T A V Y Y C A R D R S Y
ATG GAG CTG AGC AGG CTG AGA TCT GAC GAC ACG GCC GTG TAT TAC TGT GCG AGA GAT CGA TCG TAT

CDR3 - IMGT 115 120 125
P G R N Y F D Y W G Q G T L V T
CCG GGA AGG AAC TAC TTT GAC TAC TGG GGC CAG GGA ACC CTG GTC ACC

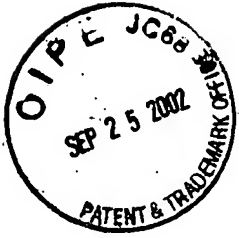


FIG. 58 Translation of CB2i-E12 kappa chain:

<----- F R 1 - I M G T ----->

1 5 10 15 20
E I V L T Q S P G T L S L S P G E R A T L S
GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA GCC ACC CTC TCC

<----->

25 30 35 40
C R A S Q S V S S S Y L A W Y Q Q
TGC AGG GCC AGT CAG AGT GTT AGC AGC AGC TAC ... TTA GCC TGG TAC CAG CAG

F R 2 - I M G T ----->

45 50 55 60 65
K P G Q A P R L L I Y G A S
AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC ... AGC

70 75 80 85
R A T G I P D R F S G S G S G T D F T
AGG GCC ACT GGC ATC CCA ... GAC AGG TTC AGT GGC AGT GGG ... TCT GGG ACA GAC TTC ACT

<----->

90 95 100 105 110
L T I S R L E P E D F A V Y Y C Q Q Y G S S
CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA GTG TAT TAC TGT CAG CAG TAT GGT AGC TCT

115
H T F G Q G
CAC ACT TTT GGC CAG GGG



FIG. 59

Translation of CB2i-E7 Heavy Chain:

<----- F R 1 - I M G T ----->

1 5 10 15 20
x G L V K P G G S L R L S
... .GA ... GGC TTG GTC AAG CCT GGA GGG TCC CTG AGA CTC TCC

<----->

CDR1 - IMGT 35 40
25 30 35 40
C A A S G F T F S D Y Y M S W I R Q
TGT GCA GCC TCT GGA TTC ACC TTC AGT GAC TAC TAC ATG AGC TGG ATC CGC CAG

F R 2 - I M G T ----->

CDR2 - IMGT 60 65
45 50 55 60 65
A P G K G L E W V S Y I S S S Y T N
GCT CCA GGG AAG GGG CTG GAG TGG GTT TCA TAC ATT AGT AGT AGT TAC ACA AAC

<----- F R 3 - I M G T ----->

70 75 80 85
Y A D S V K G R F T I S R D N A K N S L Y
TAC GCA GAC TCT GTG AAG ... GGC CGA TTC ACC ATC TCC AGA GAC AAC GCC AAG AAC TCA CTG TAT

<----->

90 95 100 105 110
L Q M N S L R A E D T A V Y Y C A R D R S S
CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC ACG GCT GTG TAT TAC TGT GCG AGA GAT CGG TCG AGC

CDR3 - IMGT 115 120 125
S S W Y Y Y Y G M D V W G Q G
AGC AGC TGG TAC TAC TAC TAC TAC GGT ATG GAC GTC TGG GGC CAA GGG



FIG. 60 Translation of CB2i-E7 kappa Chain:

<----- F R 1 - I M G T ----->

1 5 10 15 20
D I Q M T Q S P S L S A S V G D R V T I T
GAC ATC CAG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA GTC ACC ATC ACT

<----->

25 30 35 40
C R A S Q G I S N Y L A W Y Q Q
TGC CGG GCG AGT CAG GGC ATT AGC AAT TAT ... TTA GCC TGG TAT CAG CAG

F R 2 - I M G T ----->

45 50 55 60 65
K P G K V P K L L I Y A A S T
AAA CCA GGG AAA GTT CCT AAG CTC CTG ATC TAT GCT GCA TCC ... ACT

<----->

70 75 80 85
L Q S G V P S R F N G S G S G T D F T
TTG CAA TCA GGG GTC CCA ... TCT CGG TTC AAT GGC AGT GGA ... TCT GGG ACA GAT TTC ACT

<----->

90 95 100 105 110
L T I S S L Q P E D V A T Y Y C Q K Y N K C
CTC ACC ATC AGC AGC CTG CAA CCT GAA GAT GTT GCA ACT TAT TAC TGT CAA AAG TAT AAC AAG TGC

115
P S H F R G R D
CCC TCT CAC TTT CGG GGG AGG GAC

FIG. 61

Translation of MSI 19-E5 Light Chain

```

<----- F R I - I M G T ----->
      5      10      15      20
1  D I A M T Q S P D S L A V S L G E R A T I N
   GAC ATC GCG ATG ACC CAG TCT CCA GAC TCC CTG GCA GTG TCT CTG GGC GAG AGG GCC ACC ATC AAC

----->
      25      30      35      40
C  K S S R S V L F S S N N N Y L A W Y Q Q
   TGC AAG TCC AGC CGG AGT GTT TTA TTC AGC TCC AAC AAT AAC TAC TTA GCT TGG TAC CAG CAG

F R 2 - I M G T ----->
      45      50      55      60      65
K  P G Q P P K L L I Y W A S
   AAA CCA GGA CAG CCT CCT AAG CTA CTC ATT TAC TGG GCA TCT ... ACC

      CDR1 - IMGT      CDR2 - IMGT
      30      35      40      45
F R 2 - I M G T ----->
      50      55      60      65
K  P G Q P P K L L I Y W A S
   AAA CCA GGA CAG CCT CCT AAG CTA CTC ATT TAC TGG GCA TCT ... ACC

      CDR1 - IMGT      CDR2 - IMGT
      70      75      80      85
R  E S G V P D R F S G S G
   CGG GAA TCC GGG GTC CCT ... GAC CGA TTC AGT GGC AGC GGG ... TCT GGG ACA GAT TTC ACT

      CDR3 - I
      90      95      100      105      110
L  T I S S L Q A E D V A V Y Y C Q Q Y Y S T
   CTC ACC ATC AGC AGC CTG CAG GCT GAA GAT GTG GCA GTT TAT TAC TGT CAG CAA TAT TAT AGT ACT

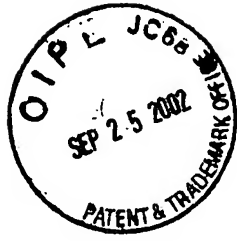
MGT
P I T F G
CCA ATC ACC TTC GGC

```



FIG. 62

Translation of 04 kappa chain 2:



```

<----- F R 1 - I M G T -----
1      5      10      15      20
D I V M T Q S H K F M S T S V G D R V S I T
GAC ATC GTA ATG ACG CAG TCT CAC AAA TTC ATG TCC ACT TCA GTA GGA GAC AGG GTC AGC ATC ACC

----->
          CDR1 - IMGT
          25      30      35      40
C K A S Q D V S T A          V A W Y Q Q
TGC AAG GCC AGT CAG GAT GTG AGT ACT GCT ... .. GTA GCC TGG TAT CAA CAG

F R 2 - I M G T ----->
          CDR2 - IMGT
          45      50      55      60
K P G Q S P K L L I Y S A S          Y
AAA CCA GGA CAA TCT CCT CCA CTA CTG ATT TAC TCG GCA TCC ... .. TAC

----- F R 3 - I M G T -----
          CDR3 - IMGT
          70      75      80      85
R Y T G V P D R F T G S G          S G T D F T
CGG TAC ACT GGA GTC CCT ... GAT CGC TTC ACT GGC AGT GGA ... TCT GGG ACG GAT TTC ACT

----->
          CDR3 - IMGT
          90      95      100      105      110
F T I S S V Q A E D L A V Y Y C Q Q H Y T T
TTC ACC ATC AGC AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT ACT ACT

          115
P L T F G A G
CCG CTC ACG TTC GGT GCT GGG

```




FIG. 63A

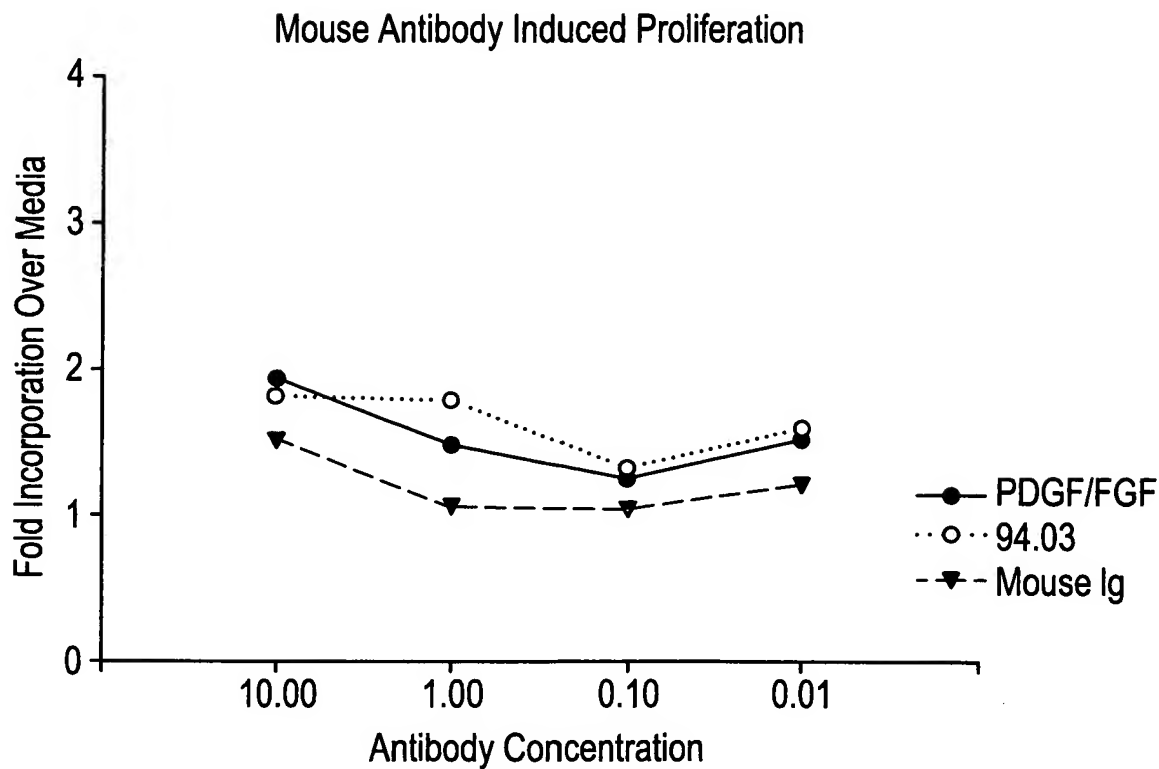


FIG. 63B

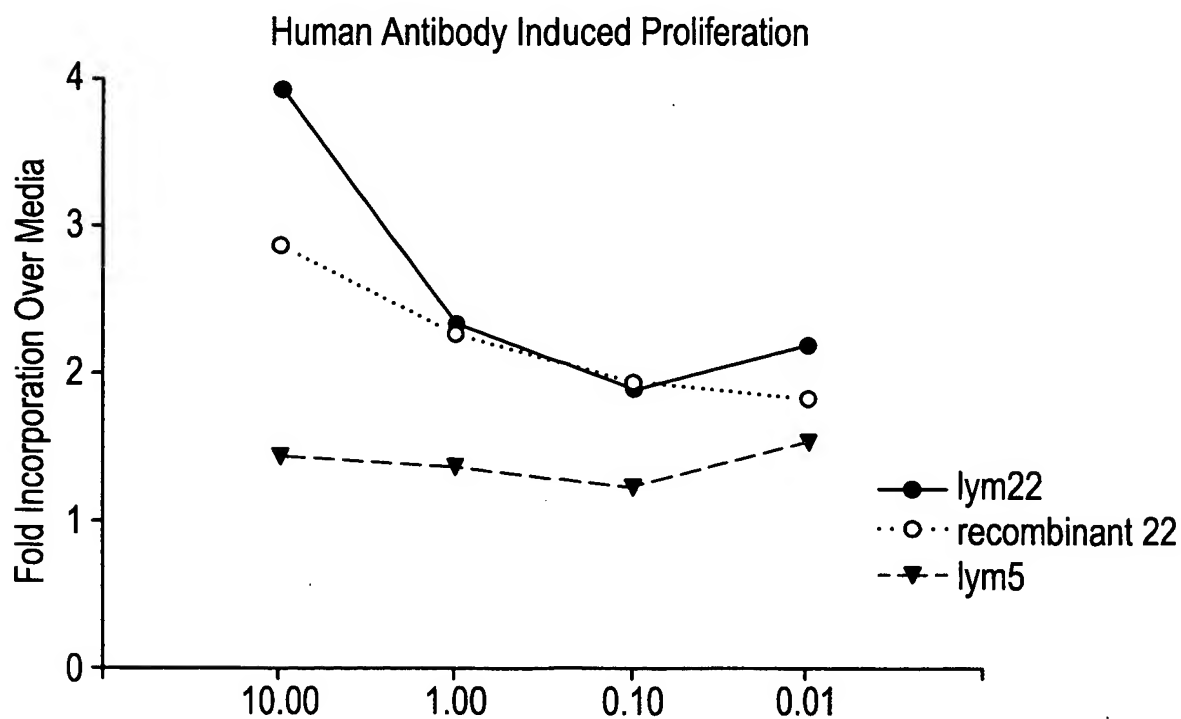
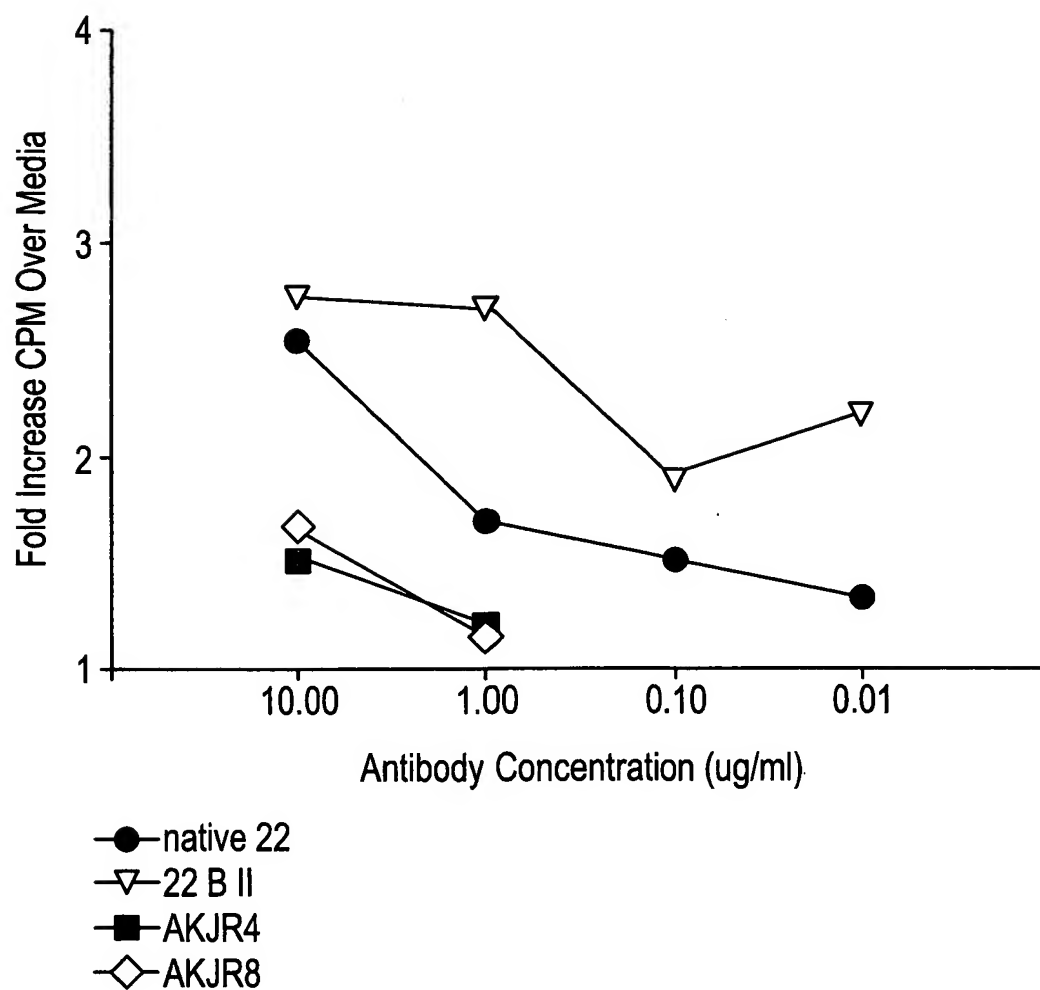
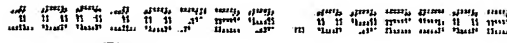




FIG. 64

Human Antibody Induced ^3H Thymidine Incorporation





Mouse Antibody Induced ³H Thymidine Incorporation

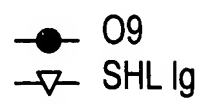
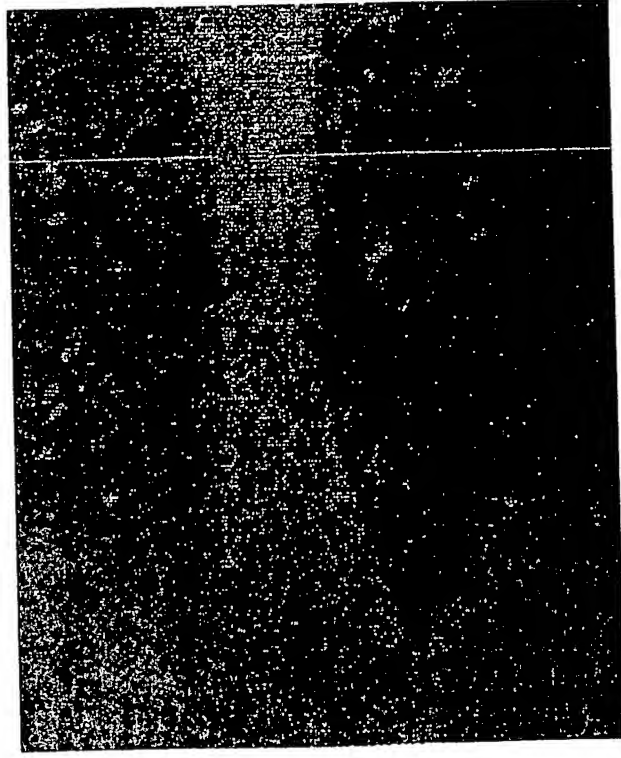
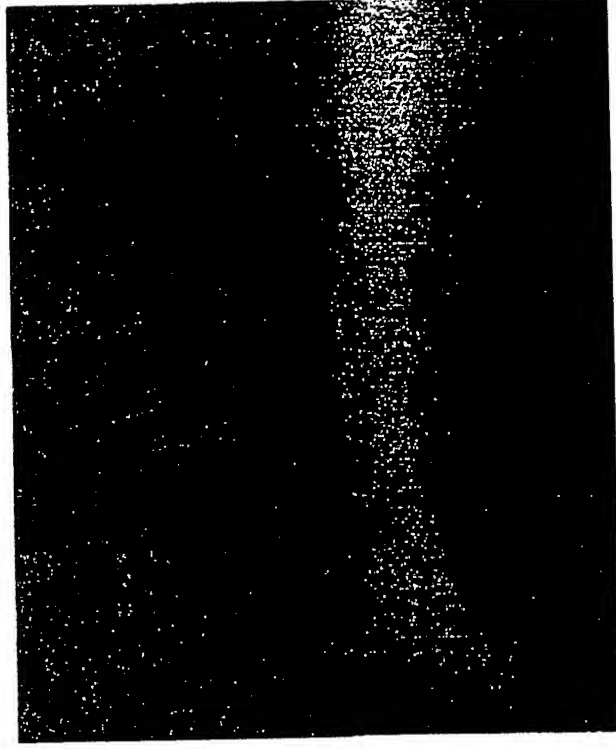


FIG. 66A



sHlgM 22

FIG. 66B



rHlgM 22



FIG. 68

TRANSLATION OF O1 KAPPA CHAIN

<----- F R 1 - I M G T ----->

1 5 10 15 20
D V Q I T Q S P S Y L A A S P G E T I T I N
GAT GTC CAG ATA ACC CAG TCT CCA TCT TAT CTT GCT GCA TCT CCT GGA GAA ACC ATT ACT ATT AAT

<----->

25 30 35 40
C R A S K S I S K Y L A W Y Q E
TGC AGG GCA AGT AAG AGC ATT AGC AAA TAT ... TTA GCC TGG TAT CAA GAG

<----->

45 50 55 60 65
K P G K T N K L I Y S G S T
AAA CCT GGG AAA ACT AAT AAG CTT CTT ATC TAC TCT GGA TCC ... ACT

<----->

70 75 80 85
L Q S G I P S R F S G S G S G T D F T
TTG CAA TCT GGA ATT CCA ... TCA AGG TTC AGT GGC AGT GGA ... TCT GGT ACA GAT TTC ACT

<----->

90 95 100 105 110
L T I S S L E P E D F A M Y Y C Q Q H N E Y
CTC ACC ATC AGT AGC CTG GAG CCT GAA GAT TTT GCA ATG TAT TAC TGT CAA CAG CAT AAT GAA TAC

<----->

115 120
P Y T F G G G T K L E I K R
CCG TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG



FIG. 69

TRANSLATION OF HNK-1 KAPPA CHAIN

<----- F R I - I M G T ----->

1 5 10 15 20
D I Q M T Q S P S L S A S L G E R V S L T
GAC ATC CAG ATG ACC CAG TCT CCA TCC TTA TCT GCC TCT CTG GGA GAA AGA GTC AGT CTC ACT

<----->

25 30 35 40
C R A S Q D I G S S L N W L Q Q
TGT CGG GCA AGT CAG GAC ATT GGT AGT AGC ... TTA AAC TGG CTT CAG CAG

F R 2 - I M G T -----> CDR1 - IMGT CDR2 - IMGT <----->

45 50 55 60 65
E P D G T I K R L I Y A T S
GAA CCA GAT GGA ACT ATT AAA CGC CTG ATC TAC GCC ACA TCC ... AGT

----- F R 3 - I M G T ----->

70 75 80 85
L D S G V P K R F S G S R S G S D Y S
TTA GAT TCT GGT GTG CCC ... AAA AGG TTC AGT GGC AGT AGG ... TCT GGG TCA GAT TAT TCT

<----->

90 95 100 105 110
L T I S S L E S E D F V D Y Y C L Q Y A S
CTC ACC ATC AGC AGC CTT GAG TCT GAA GAT TTT GTA GAC TAT TAC TGT CTA CAA TAT GCT AGT TTT

----->

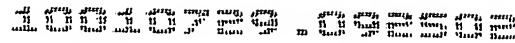
115 120
P Y T F G G G T K L E I K R
CCG TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG



FIG. 70

TRANSLATION OF A2B5 KAPPA CHAIN

←-----> F R 1 - I M G T ----->
1 5 10 15 20
Q I V L T Q S P A I M S A S P G E K V T I S
CAA ATT GTT CTC ACC CAG TCT CCA GCA ATC ATG TCT GCA TCT CCA GGG GAG AAG GTC ACC ATA TCC
-----> <----->
25 30 35 40
C S A S S S V S Y M Y W Y Q Q
TGC AGT GCC AGC TCA AGT GTA AGT TAC ... ATG TAC TGG TAC CAG CAG
F R 2 - I M G T -----> <----->
45 50 55 60 65
K P G S S P K P W I Y R T S N
AAG CCA GGA TCC TCC CCC AAA CCC TGG ATT TAT CGC ACA TCC ... AAC
-----> F R 3 - I M G T ----->
70 75 80 85
L A S G V P A R F S G S G T S Y S
CTG GCT TCT GGA GTC CCT ... GCT CGC TTC AGT GGC AGT GGG ... TCT GGG ACC TCT TAC TCT
-----> <----->
90 95 100 105 110
L T I S S M E A E D A A T Y Y C Q Y H S Y
CTC ACA ATC AGC AGC ATG GAG GCT GAA GAT GCT GCC ACT TAT TAC TGC CAG CAG TAT CAT AGT TAC
-----> <----->
115 120
P L T F G A G T K L E L K R
CCA CTC ACG TTC GGT GCT GGG ACC AAG CTG GAG CTG AAA CGG



LYM 46 Heavy Chain Sequence:

T V S S
ACT GTC TCC TCA



FIG. 72

YM 46 KAPPA LIGHT CHAIN SEQUENCE:

----- F R I - I M G T -----

5 D I V M T Q S P D S L A V S L G E R A T I N
AC ATC GTG ATG ACC CAG TCT CCA GAC TCC CTG GCT GTG TCT CTG GGC GAG AGG GCC ACC ATC AAC

-----> <-----

25 C K S S Q S V L Y S S N K N Y L A W Y Q Q
GC AAG TCC AGC CAG AGT GTT TTA TAC AGC TCC AAC AAT AAG AAC TAC TTA GCT TGG TAC CAG CAG

CDR1 - IMGT 30 35 40

5 R 2 - I M G T -----> CDR2 - IMGT 55 60 65 <----

5 K P G Q P P K L L I Y W A S
AA CCA GGA CAG CCT CCT AAA CTA CTC ATT TAC TGG GCA TCT ACC

----- F R 3 - I M G T -----

70 R E S G V P D R F S G S G 80 85
GG GAA TCC GGG GTC CCT ... GAC CGA TTC AGT GGC AGC GGG ... TCT GGG ACA GAT TTC ACT

-----> <-----

90 L T I S S L Q A E D V A V Y Y C Q Q Y Y N T
TC ACC ATC AGC AGC CTG CAG GCT GAA GAT GTG GCA GTT TAT TAC TGT CAG CAA TAT TAT AAT ACT

CDR3 - IMGT 100 105 110

115 P Q A F G Q G T K V E I K R T V A A P S V F
CT CAG GCG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA CGA ACT GTG GCT GCA CCA TCT GTC TTC

120 125 130



FIG. 73

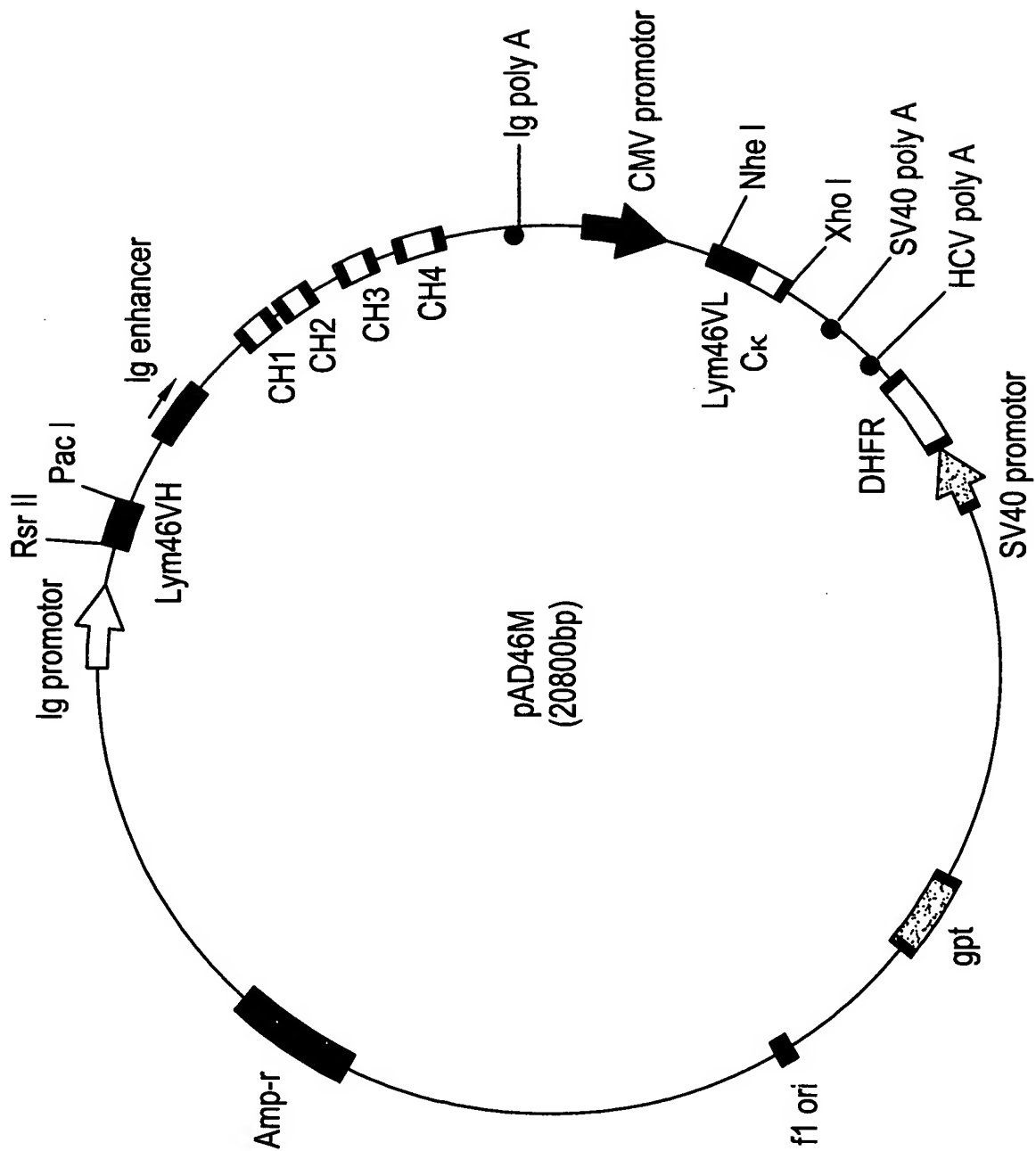




FIG. 74

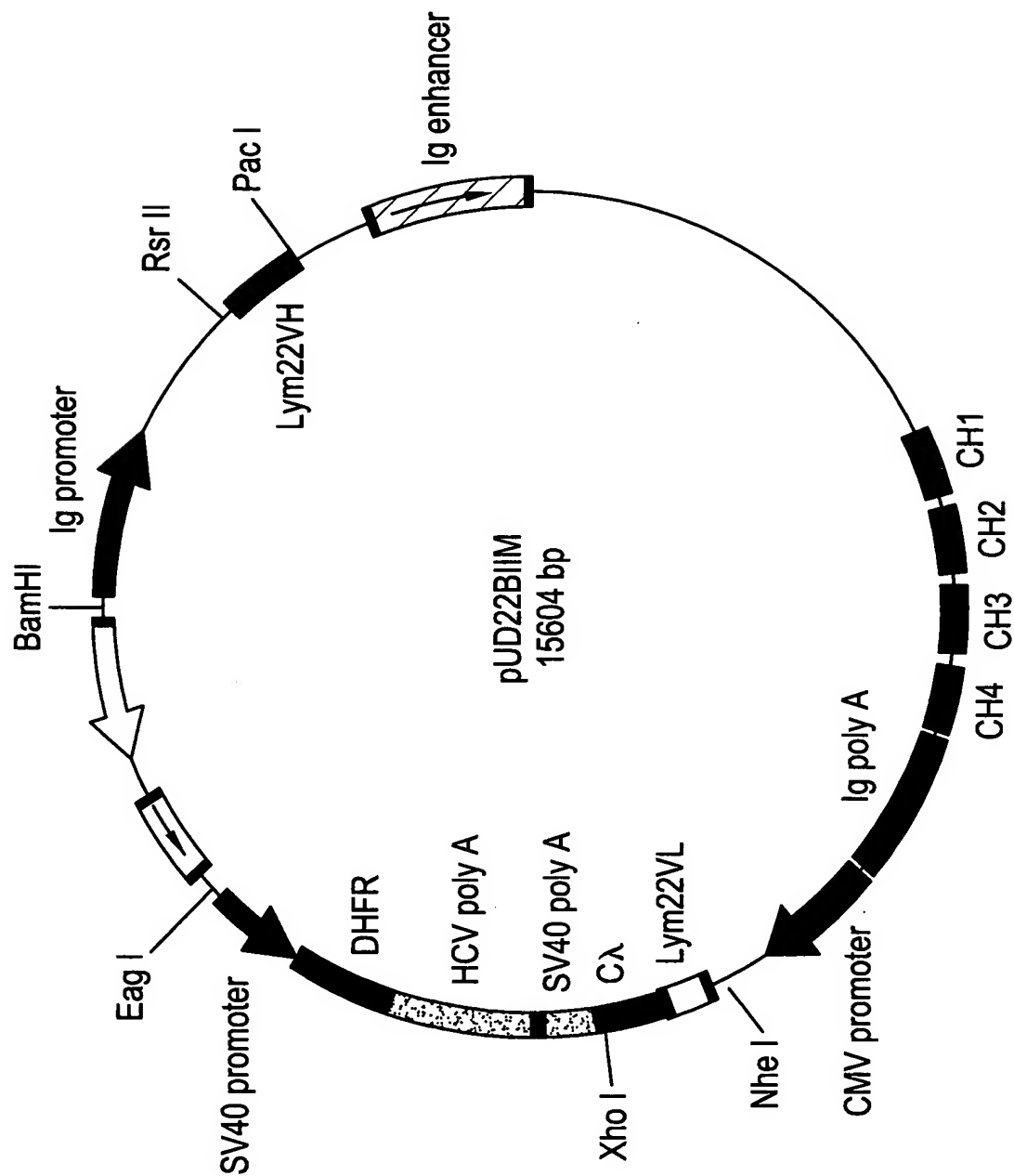




FIG. 75

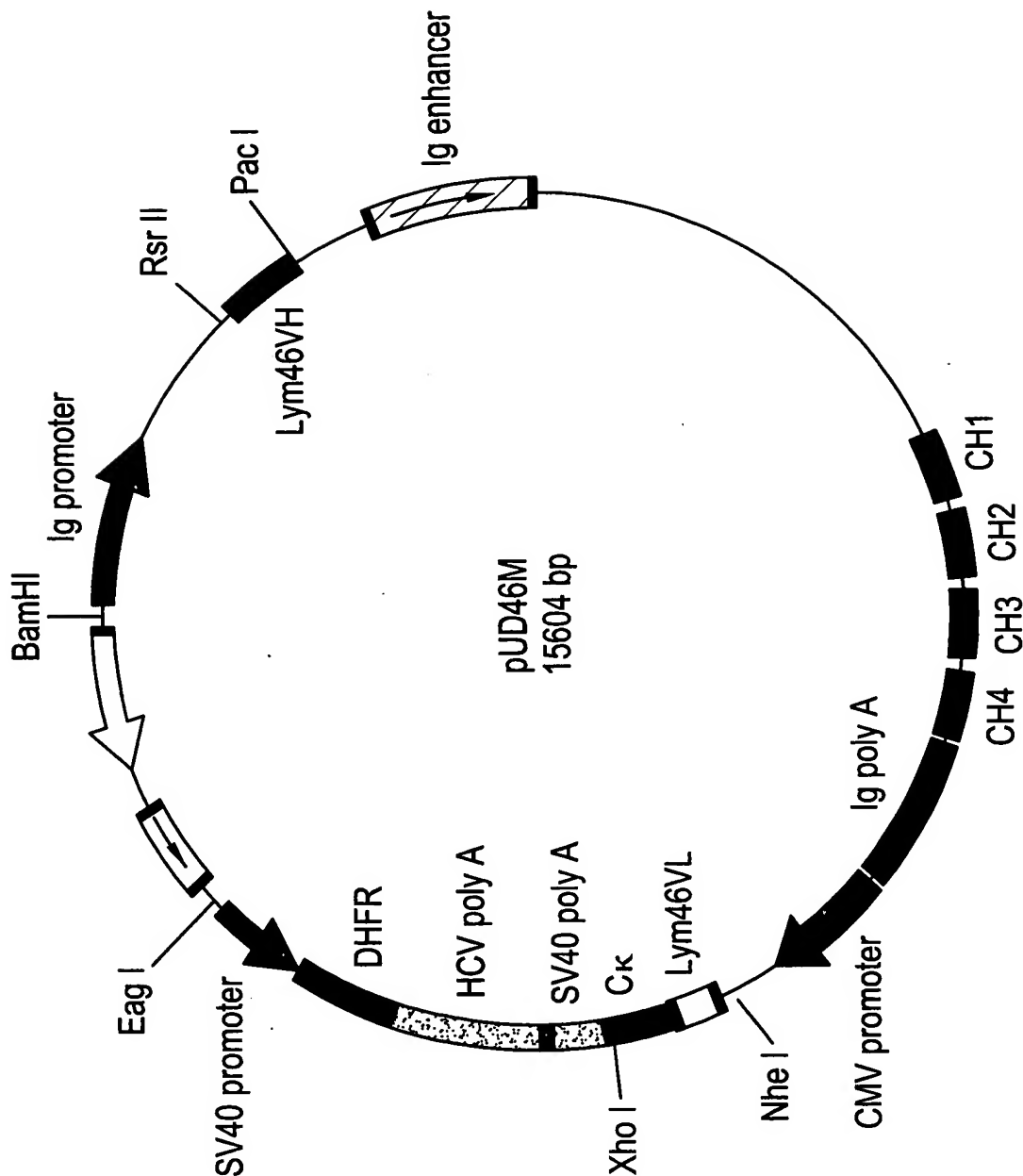


FIG. 76

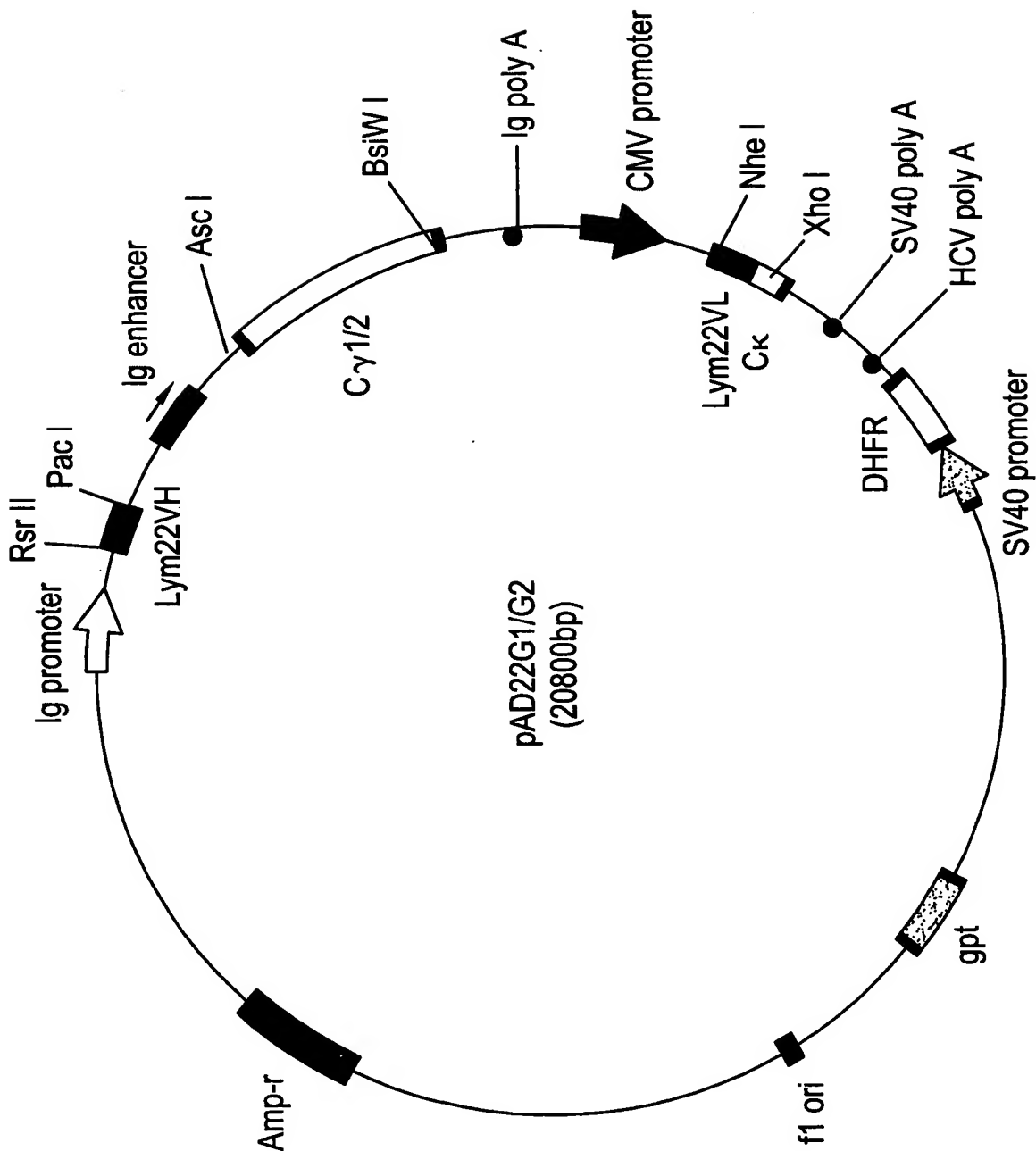




FIG. 77

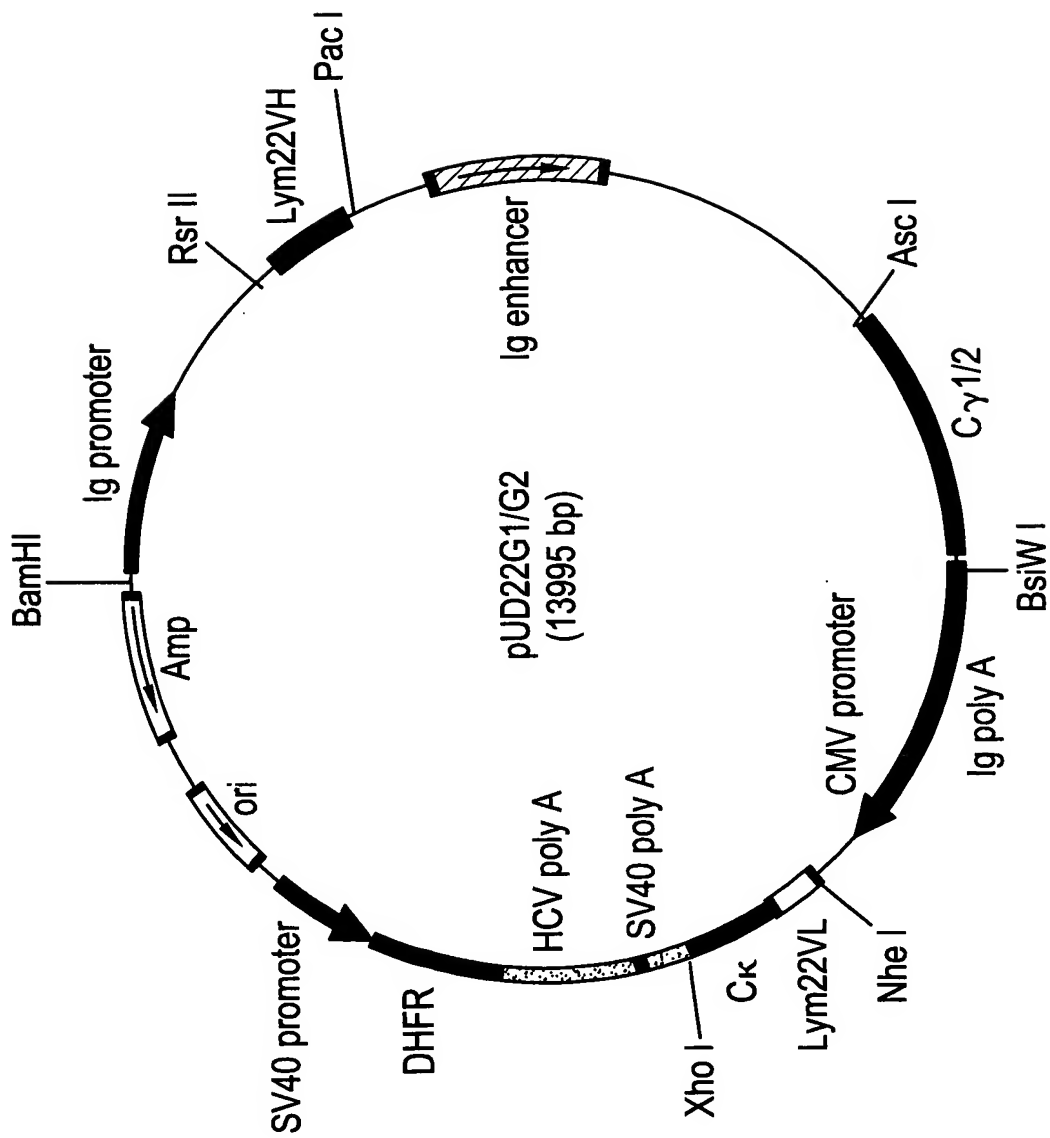




FIG. 78

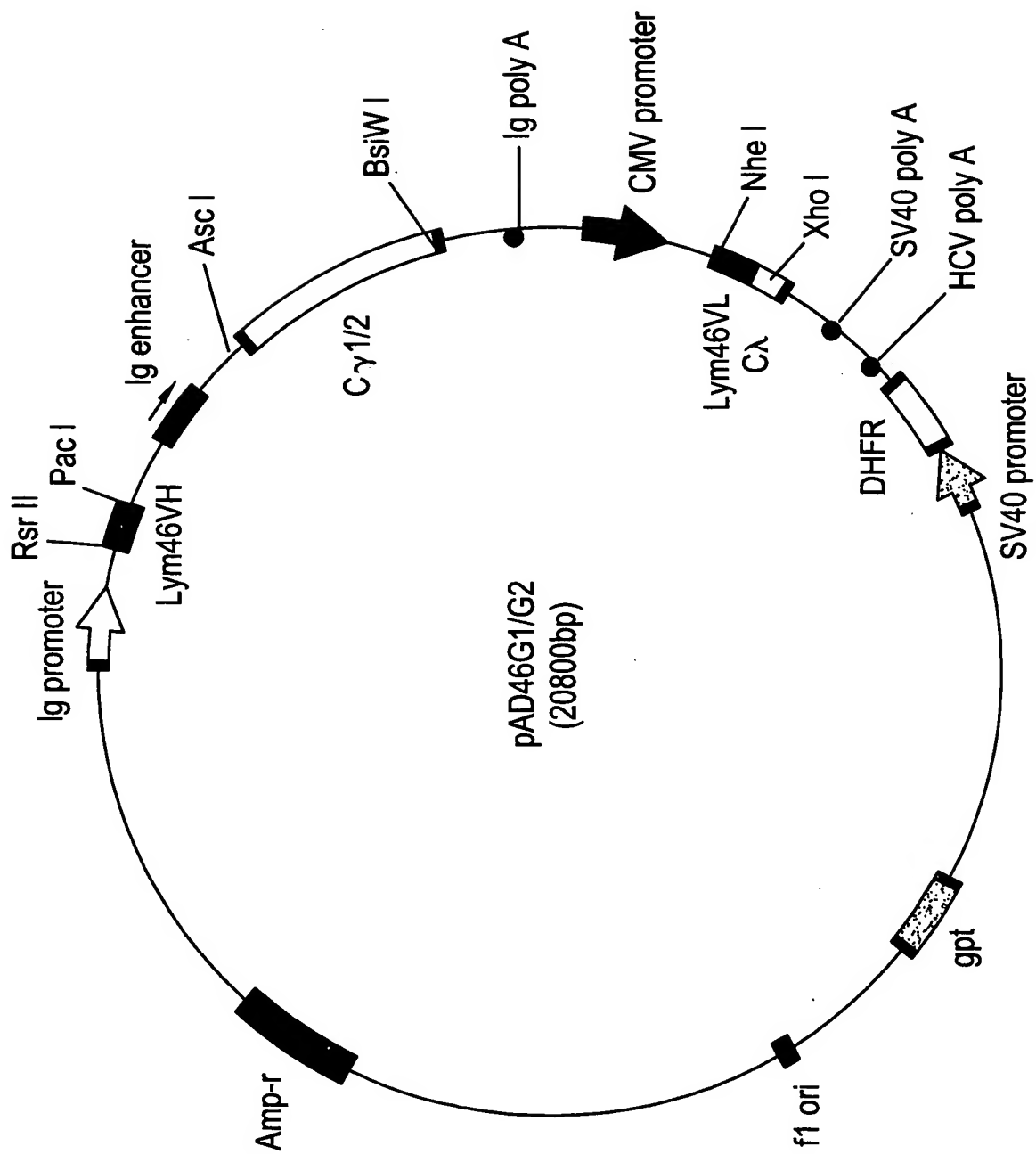
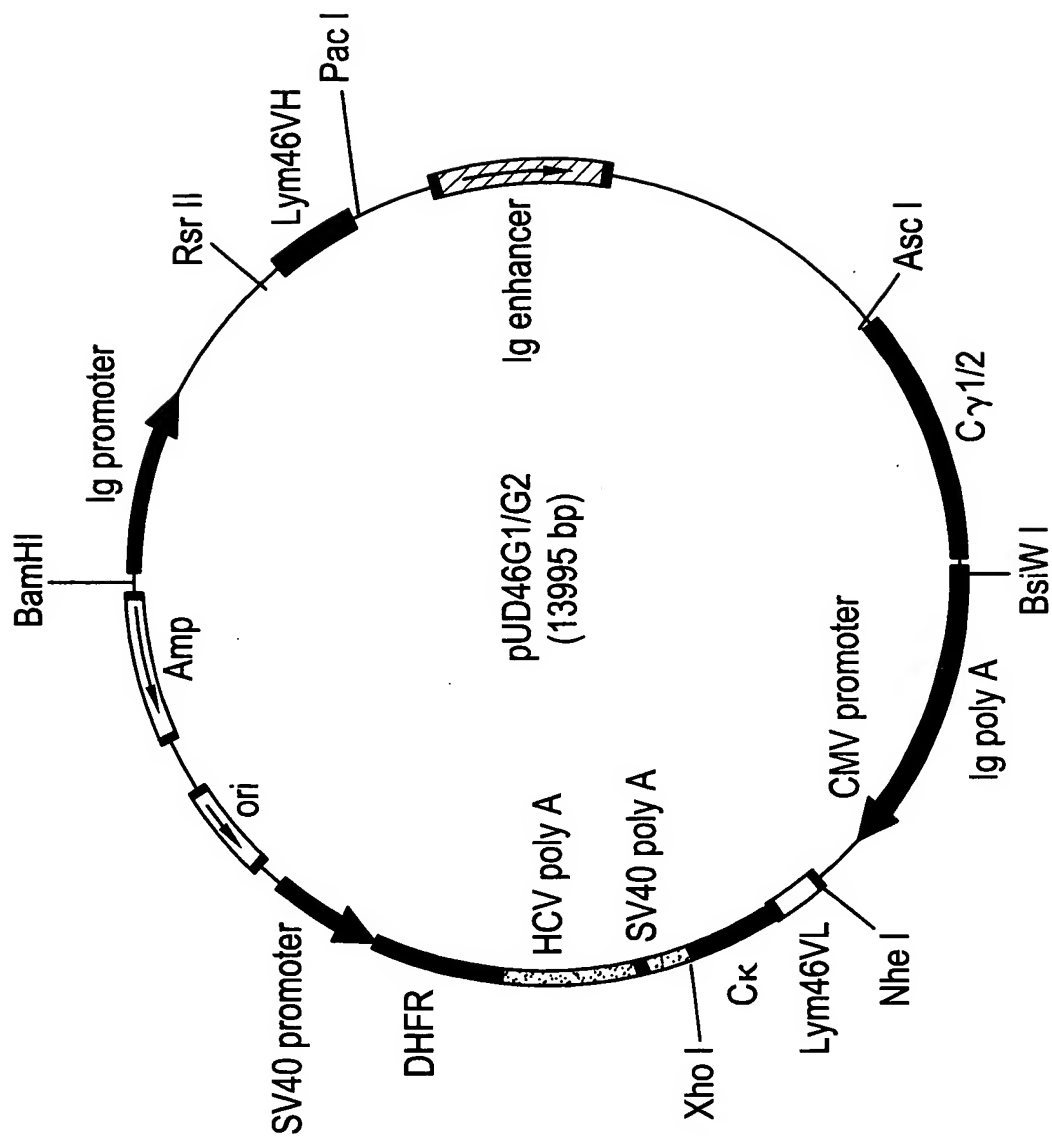




FIG. 79



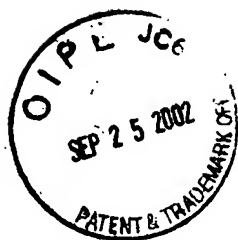


FIG. 80A

TMEV Infected SJL Mice
Treated at 21 Days Post Infection

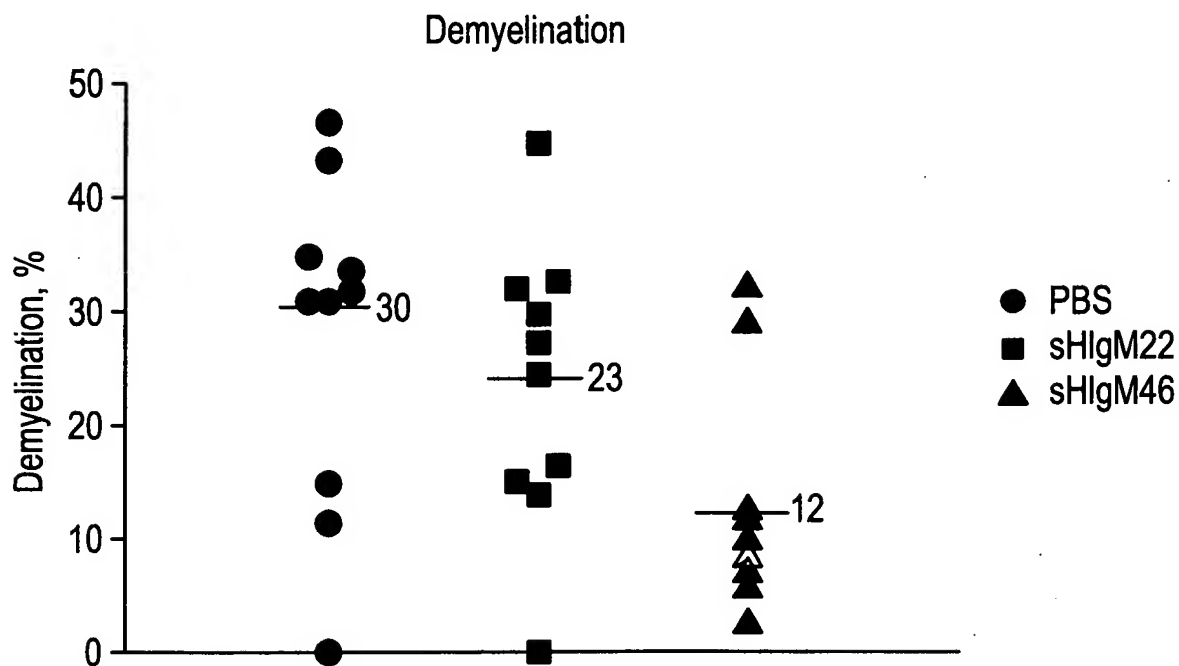
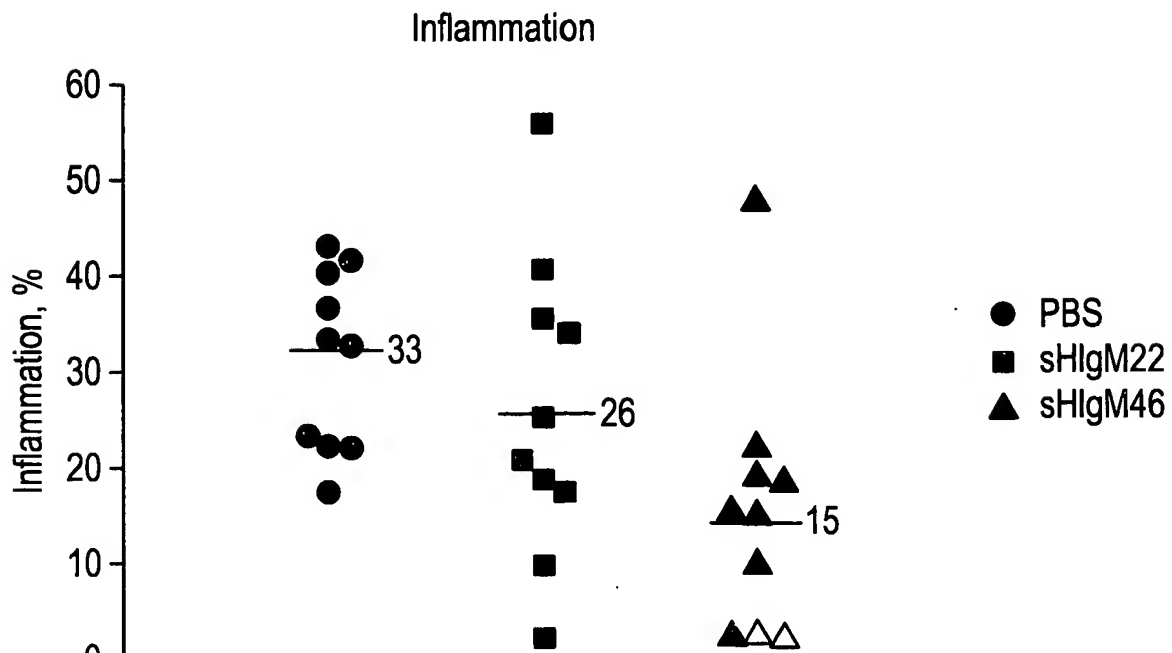
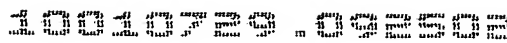


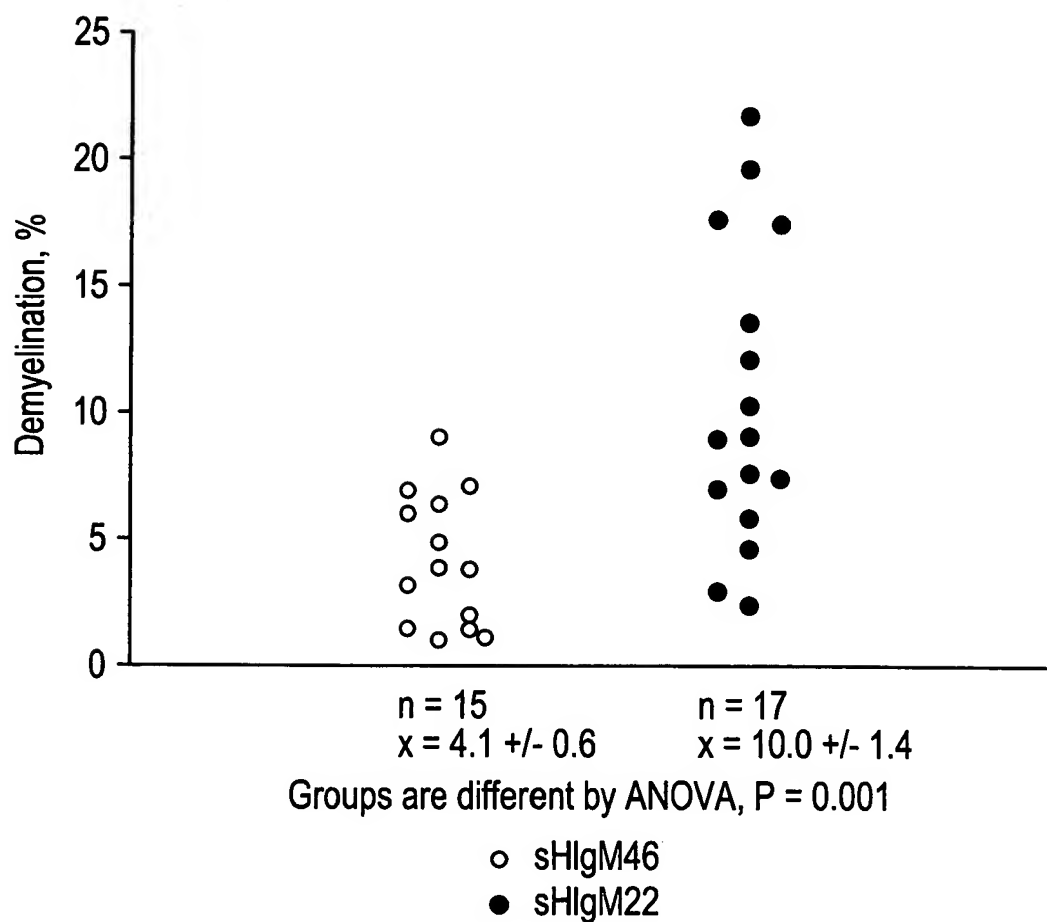
FIG. 80B

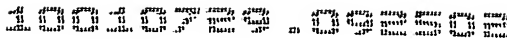
TMEV Infected SJL Mice
Treated at 21 Days Post Infection





Chronically TMEV Infected SJL Mice Treated with sHlgM46 or sHlgM22





Chronically TMEV Infected SJL Mice Treated sHlgM46 vs All Other Antibodies



- sHlgM46
- other mAbs



FIG. 83

^{45}Ca Internalization in Undif CG4 Cells

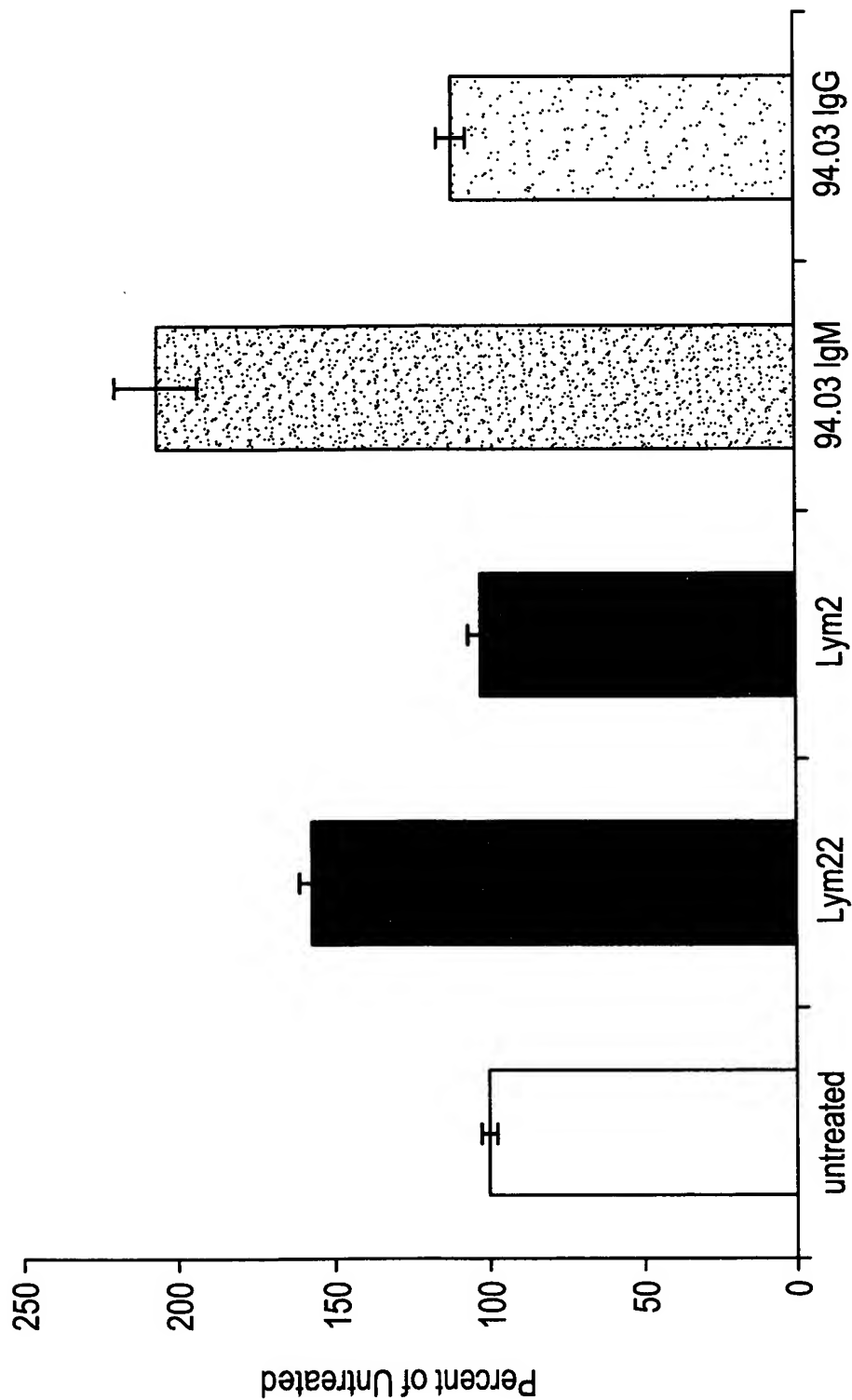
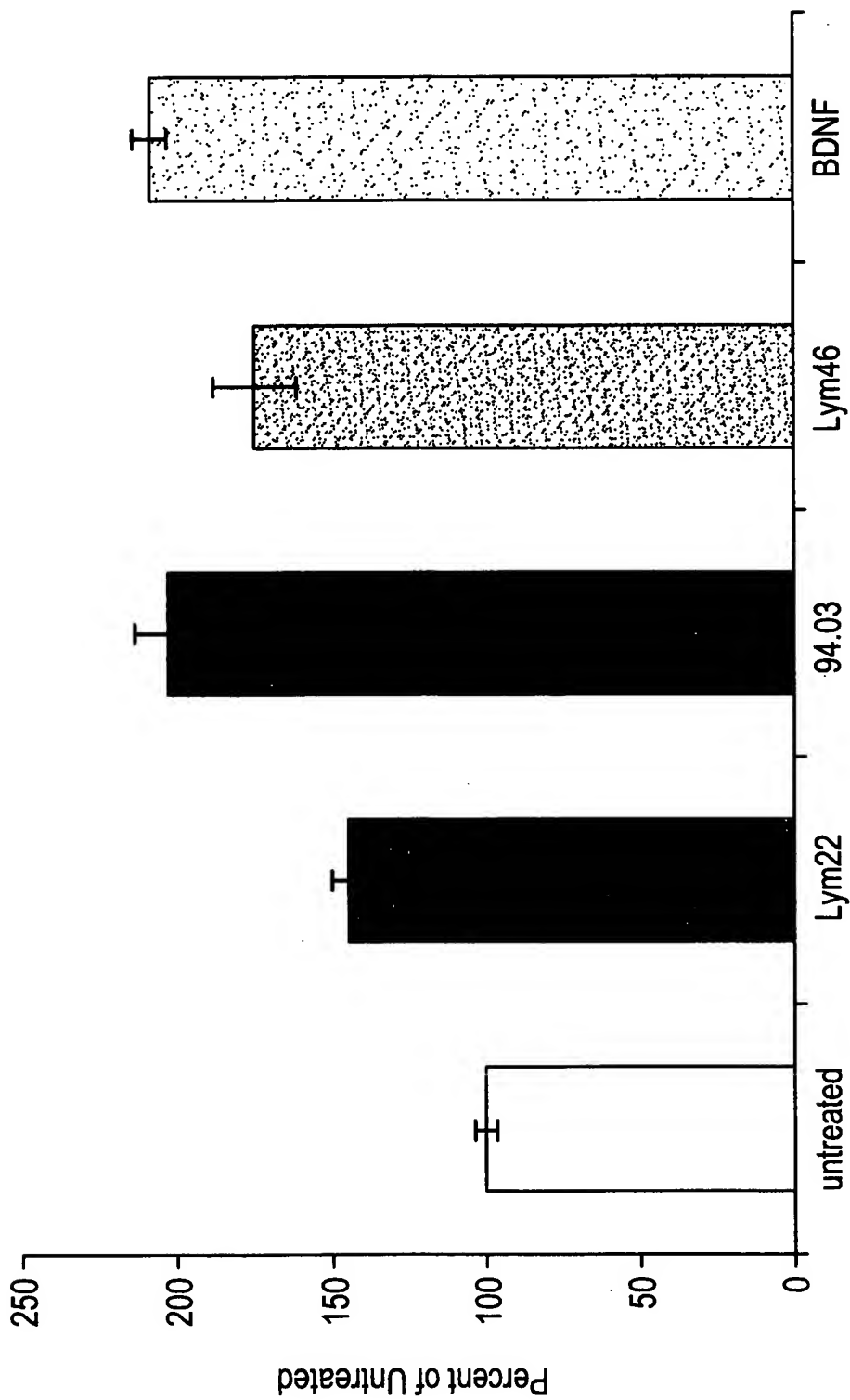




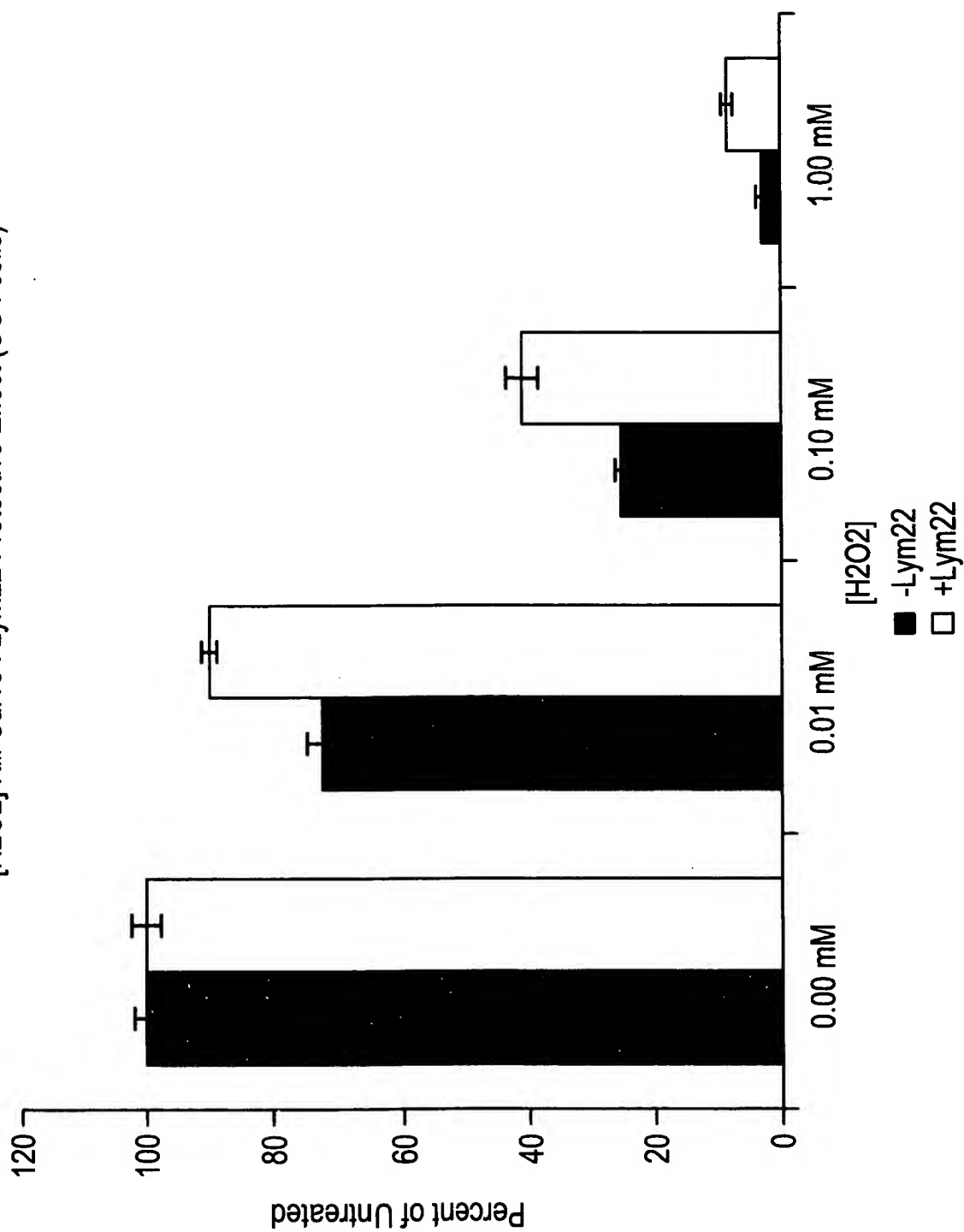
FIG. 84

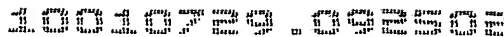
^{45}Ca Internalization in CG4 Cells



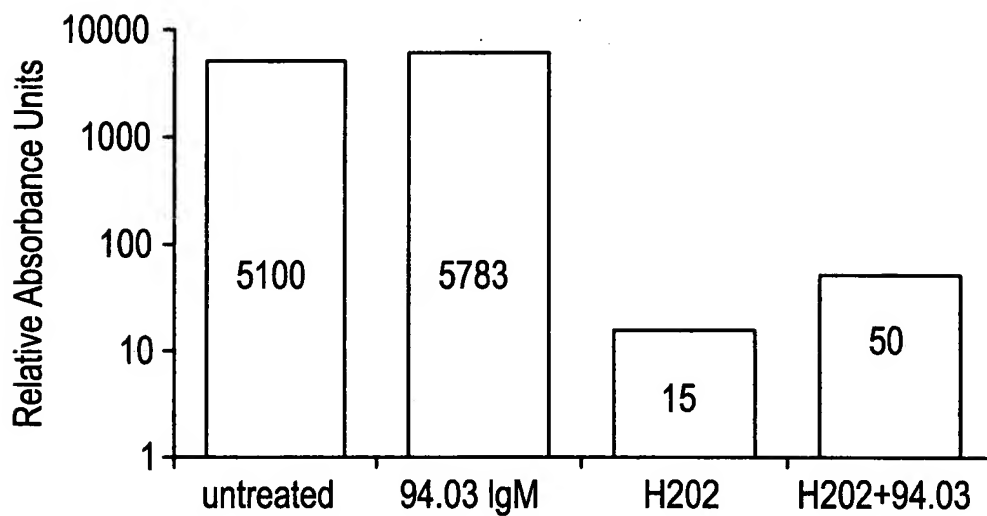


[H2O2] Kill Curve : Lym22 Protective Effect (CG4 cells)





MTT Assay: H₂O₂-induced cell death



Cell Number: H₂O₂-induced cell death

